

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: SABHA QAZI Examiner #: 74141 Date: 8/23/04
 Art Unit: 1616 Phone Number: 202 206 822 Serial Number: 10/763 023
 Mail Box and Bldg/Room Location: _____ Results Format Preferred (circle): PAPER DISK E-MAIL

4670 Rem 4445
 If more than one search is submitted, please prioritize searches in order of need.

 Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc. if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: (205) 1 alpha-hydroxy-2 alpha-... 19-nor-Vit D₃
 Inventors (please provide full names): DeLuca et al

Earliest Priority Filing Date: 4/22/2002

For Sequence Searches Only Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.

19-nor
 Please search for 19-nor-Vit D₃ compounds and methods as in cl 1

Please note that any isomer can be of treating psoriasis
 103.
 Specific method 1 is claimed.

Related cases
10/763, 029
10/762, 906
10/762, 710
10/762, 618
10/127, 180

STAFF USE ONLY

	Type of Search	Vendors and cost where applicable
Searcher: <u>Jan</u>	NA Sequence (#) _____	STN <input checked="" type="checkbox"/>
Searcher Phone #: <u>22504</u>	AA Sequence (#) _____	Dialog _____
Searcher Location: _____	Structure (#) <input checked="" type="checkbox"/>	Questel/Orbit _____
Date Searcher Picked Up: <u>8/25</u>	Bibliographic _____	Dr Link _____
Date Completed: <u>8/25</u>	Litigation _____	Lexis/Nexis _____
Searcher Prep & Review Time: _____	Fulltext _____	Sequence Systems _____
Clerical Prep Time: <u>15</u>	Patent Family _____	WWW/Internet _____
Online Time: <u>5:20</u>	Other _____	Other (specify) _____

=> fil reg

FILE 'REGISTRY' ENTERED AT 10:09:50 ON 25 AUG 2004

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PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

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STRUCTURE FILE UPDATES: 24 AUG 2004 HIGHEST RN 732209-96-0

DICTIONARY FILE UPDATES: 24 AUG 2004 HIGHEST RN 732209-96-0

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

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Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:

<http://www.cas.org/ONLINE/DBSS/registryss.html>

=> d l13 ide can tot

L13 ANSWER 1 OF 2 REGISTRY COPYRIGHT 2004 ACS on STN

RN 618104-21-5 REGISTRY

CN 1,3-Cyclohexanediol, 5-[(2E)-[(1R,3aS,7aR)-1-[(1S)-1,5-dimethylhexyl]octahydro-7a-methyl-4H-inden-4-ylidene]ethylidene]-2-methylene-, (1R,3R)- (9CI) (CA INDEX NAME)

FS STEREOSEARCH

MF C27 H44 O2

SR CA

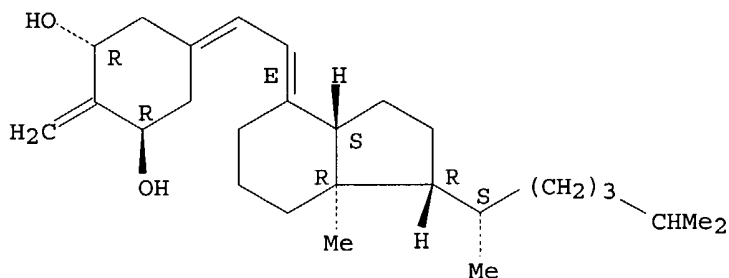
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

DT.CA Caplus document type: Patent

RL.P Roles from patents: PREP (Preparation); RACT (Reactant or reagent)

Absolute stereochemistry.

Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)

1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

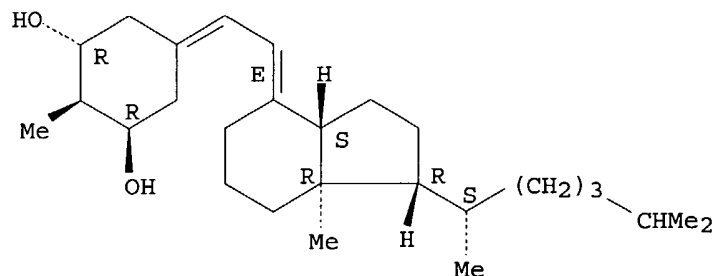
REFERENCE 1: 139:345953

L13 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2004 ACS on STN

RN 618104-20-4 REGISTRY

CN 1,3-Cyclohexanediol, 5-[(2E)-[(1R,3aS,7aR)-1-[(1S)-1,5-dimethylhexyl]octahydro-7a-methyl-4H-inden-4-ylidene]ethylidene]-2-methyl-, (1R,3R)-(9CI) (CA INDEX NAME)
 FS STEREOSEARCH
 MF C27 H46 O2
 SR CA
 LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL
 DT.CA Caplus document type: Patent
 RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Absolute stereochemistry.
 Double bond geometry as shown.



****PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT****

1 REFERENCES IN FILE CA (1907 TO DATE)
 1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:345953

=> fil hcaplus
 FILE 'HCAPLUS' ENTERED AT 10:09:58 ON 25 AUG 2004
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 PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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FILE COVERS 1907 - 25 Aug 2004 VOL 141 ISS 9
 FILE LAST UPDATED: 24 Aug 2004 (20040824/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

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L19 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2004 ACS on STN
 AN 2003:855808 HCAPLUS

DN 139:345953
 ED Entered STN: 31 Oct 2003
 TI (20S)-1 α -Hydroxy-2 α -methyl--19-nor-vitamin D3 and
 (20S)-1 α -hydroxy-2 β -methyl--19-nor-vitamin D3, and
 pharmaceutical uses
 IN Deluca, Hector F.; Sicinski, Rafal R.; Grzywacz, Pawel K.
 PA Wisconsin Alumni Research Foundation, USA
 SO PCT Int. Appl., 44 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 IC ICM A61K031-593
 ICS A61P017-06; A61P019-10; A61P035-00; A61P037-06
 CC 1-12 (Pharmacology)
 Section cross-reference(s): 32, 63
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003088977	A1	20031030	WO 2003-US8423	20030320
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2003203882	A1	20031030	US 2002-127180	20020422
	US 2004152675	A1	20040805	US 2004-762618	20040122
	US 2004152676	A1	20040805	US 2004-762710	20040122
	US 2004152677	A1	20040805	US 2004-762906	20040122
	US 2004152678	A1	20040805	US 2004-762911	20040122
	US 2004152679	A1	20040805	US 2004-763023	20040122
	US 2004152680	A1	20040805	US 2004-763029	20040122
PRAI	US 2002-127180	A	20020422		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2003088977	ICM	A61K031-593
	ICS	A61P017-06; A61P019-10; A61P035-00; A61P037-06

AB The invention discloses (20S)-1 α -hydroxy-2 α -methyl-19-nor-vitamin D3 and (20S)-1 α -hydroxy-2 β -methyl-19-nor-vitamin D3 and pharmaceutical uses thereof. These compds. exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte, thus evidencing use as an anticancer agent and for the treatment of skin diseases, e.g. psoriasis, as well as skin conditions such as wrinkles, slack skin, dry skin and insufficient sebum secretion. These compds. also have very significant calcemic activity and therefore may be used to treat immune disorders in humans as well as metabolic bone diseases, e.g. osteoporosis. Compound preparation is described.

ST norvitamin D3 deriv prepn therapeutic; antitumor skin condition therapy norvitamin D3 deriv; immune disease osteoporosis norvitamin D3 deriv; metabolic bone disease norvitamin D3 deriv

IT Animal cell line
 (HL-60; nor-vitamin D3 derivs. and pharmaceutical uses)

IT Bone
 (bone mass increase; nor-vitamin D3 derivs. and pharmaceutical uses)

IT Biological transport
 (calcium; nor-vitamin D3 derivs. and pharmaceutical uses)

IT Intestine, neoplasm

(colon; nor-vitamin D3 derivs. and pharmaceutical uses)

IT Drugs
(gastrointestinal; nor-vitamin D3 derivs. and pharmaceutical uses)

IT Transplant and Transplantation
(host-vs.-graft reaction; nor-vitamin D3 derivs. and pharmaceutical uses)

IT Hydration, physiological
(inadequate dermal hydration; nor-vitamin D3 derivs. and pharmaceutical uses)

IT Cell differentiation
(inducers; nor-vitamin D3 derivs. and pharmaceutical uses)

IT Intestine, disease
(inflammatory; nor-vitamin D3 derivs. and pharmaceutical uses)

IT Sebum
(insufficient secretion; nor-vitamin D3 derivs. and pharmaceutical uses)

IT Osteoporosis
(low bone turnover osteoporosis; nor-vitamin D3 derivs. and pharmaceutical uses)

IT Anti-inflammatory agents
Antiasthmatics
Antidiabetic agents
Antirheumatic agents
Antitumor agents
Asthma
Autoimmune disease
Cell differentiation
Diabetes mellitus
Human
Inflammation
Leukemia
Lupus erythematosus
Mammary gland, neoplasm
Monocyte
Multiple sclerosis
Osteomalacia
Prostate gland, neoplasm
Psoriasis
Rheumatoid arthritis
Transplant rejection
(nor-vitamin D3 derivs. and pharmaceutical uses)

IT Vitamin D receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(nor-vitamin D3 derivs. and pharmaceutical uses)

IT Drug delivery systems
(oral; nor-vitamin D3 derivs. and pharmaceutical uses)

IT Bone, disease
(osteopenia; nor-vitamin D3 derivs. and pharmaceutical uses)

IT Drug delivery systems
(parenterals; nor-vitamin D3 derivs. and pharmaceutical uses)

IT Osteoporosis
(postmenopausal; nor-vitamin D3 derivs. and pharmaceutical uses)

IT Myelocyte
(promyelocyte; nor-vitamin D3 derivs. and pharmaceutical uses)

IT Aging, animal
(senile osteoporosis; nor-vitamin D3 derivs. and pharmaceutical uses)

IT Steroids, biological studies
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(steroid-induced osteoporosis; nor-vitamin D3 derivs. and pharmaceutical uses)

IT Drug delivery systems
(topical; nor-vitamin D3 derivs. and pharmaceutical uses)

IT Drug delivery systems

(transdermal; nor-vitamin D3 derivs. and pharmaceutical uses)

IT Skin
(wrinkles and other conditions; nor-vitamin D3 derivs. and pharmaceutical uses)

IT 7440-70-2, Calcium, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(nor-vitamin D3 derivs. and pharmaceutical uses)

IT **618104-20-4P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(nor-vitamin D3 derivs. and pharmaceutical uses)

IT 50-14-6, Vitamin D2 98-59-9, p-Toluenesulfonyl chloride 98-88-4, Benzoyl chloride 4237-74-5 213250-64-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(nor-vitamin D3 derivs. and pharmaceutical uses)

IT 64190-52-9P 66774-70-7P 66774-71-8P 115527-12-3P 145354-28-5P 235108-01-7P 235108-02-8P **618104-21-5P** 618104-22-6P 618879-43-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(nor-vitamin D3 derivs. and pharmaceutical uses)

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Bouillon, R; ENDOCRINE REVIEWS 1995, V16(2), P200 HCAPLUS

(2) Castedo, L; TETRAHEDRON LETTERS 1986, V27(13), P1523 HCAPLUS

(3) Deluca, H; US 6306844 B1 2001 HCAPLUS

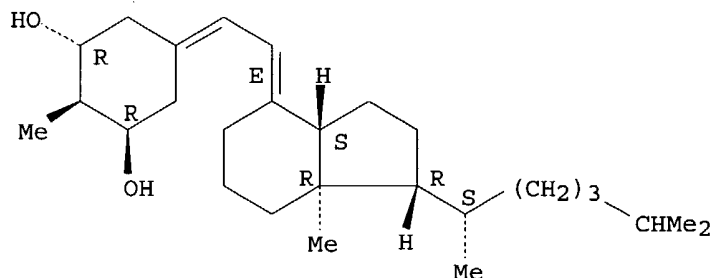
(4) Sicinski; JOURNAL OF MEDICINAL CHEMISTRY 1998, V41, P4662 HCAPLUS

IT **618104-20-4P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(nor-vitamin D3 derivs. and pharmaceutical uses)

RN 618104-20-4 HCAPLUS

CN 1,3-Cyclohexanediol, 5-[(2E)-[(1R,3aS,7aR)-1-[(1S)-1,5-dimethylhexyl]octahydro-7a-methyl-4H-inden-4-ylidene]ethylidene]-2-methyl-, (1R,3R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



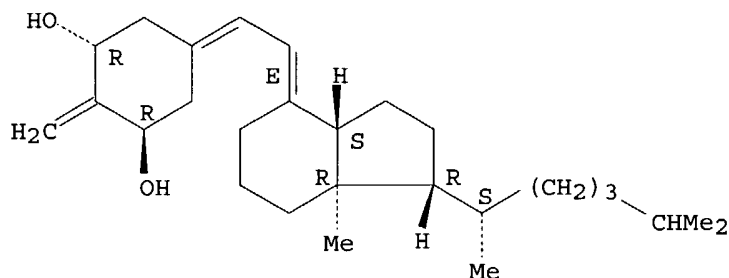
IT **618104-21-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(nor-vitamin D3 derivs. and pharmaceutical uses)

RN 618104-21-5 HCAPLUS

CN 1,3-Cyclohexanediol, 5-[(2E)-[(1R,3aS,7aR)-1-[(1S)-1,5-dimethylhexyl]octahydro-7a-methyl-4H-inden-4-ylidene]ethylidene]-2-methylene-, (1R,3R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



=> fil uspatall

FILE 'USPATFULL' ENTERED AT 10:10:13 ON 25 AUG 2004

CA INDEXING COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'USPAT2' ENTERED AT 10:10:13 ON 25 AUG 2004

CA INDEXING COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

=> d bib abs hitstr tot l20

L20 ANSWER 1 OF 7 USPATFULL on STN

AN 2004:197374 USPATFULL

TI (20S)-1 α -hydroxy-2 α -methyl and 2 β -methyl-19-nor-vitamin D₃ and their uses

IN DeLuca, Hector F., Deerfield, WI, UNITED STATES

Sicinski, Rafal R., Warsaw, POLAND

Grzywacz, Pawel K., Madison, WI, UNITED STATES

PA Wisconsin Alumni Research Foundation, Madison, WI (U.S. corporation)

PI US 2004152680 A1 20040805

AI US 2004-763029 A1 20040122 (10)

RLI Division of Ser. No. US 2002-127180, filed on 22 Apr 2002, PENDING

DT Utility

FS APPLICATION

LREP ANDRUS, SCEALES, STARKE & SAWALL, LLP, 100 EAST WISCONSIN AVENUE, SUITE 1100, MILWAUKEE, WI, 53202

CLMN Number of Claims: 77

ECL Exemplary Claim: 1

DRWN 1 Drawing Page(s)

LN.CNT 981

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention discloses (20S)-1 α -hydroxy-2 α -methyl-19-nor-vitamin D₃ and (20S)-1 α -hydroxy-2 α -methyl-19-nor-vitamin D₃ and pharmaceutical uses therefor. These compounds exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as an anti-cancer agent and for the treatment of skin diseases such as psoriasis as well as skin conditions such as wrinkles, slack skin, dry skin and insufficient sebum secretion. These compounds also have very significant calcemic activity and therefore may be used to treat immune disorders in humans as well as metabolic bone diseases such as osteoporosis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

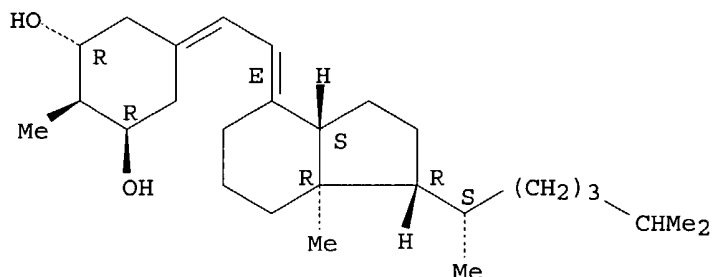
IT 618104-20-4P

(nor-vitamin D₃ derivs. and pharmaceutical uses)

RN 618104-20-4 USPATFULL

CN 1,3-Cyclohexanediol, 5-[(2E)-[(1R,3aS,7aR)-1-[(1S)-1,5-dimethylhexyl]octahydro-7a-methyl-4H-inden-4-ylidene]ethylidene]-2-methyl-, (1R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



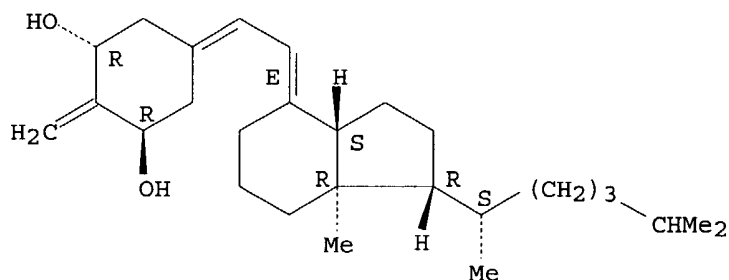
IT 618104-21-5P

(nor-vitamin D3 derivs. and pharmaceutical uses)

RN 618104-21-5 USPATFULL

CN 1,3-Cyclohexanediol, 5-[(2E)-[(1R,3aS,7aR)-1-[(1S)-1,5-dimethylhexyl]octahydro-7a-methyl-4H-inden-4-ylidene]ethylidene]-2-methylene-, (1R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L20 ANSWER 2 OF 7 USPATFULL on STN

AN 2004:197373 USPATFULL

TI (20S)-1alpha-hydroxy-2alpha-methyl and 2beta-methyl-19-nor-vitamin D3 and their uses

IN DeLuca, Hector F., Deerfield, WI, UNITED STATES

Sicinski, Rafal R., Warsaw, POLAND

Grzywacz, Pawel K., Madison, WI, UNITED STATES

PA Wisconsin Alumni Research Foundation, Madison, WI (U.S. corporation)

PI US 2004152679 A1 20040805

AI US 2004-763023 A1 20040122 (10)

RLI Division of Ser. No. US 2002-127180, filed on 22 Apr 2002, PENDING

DT Utility

FS APPLICATION

LREP ANDRUS, SCEALES, STARKE & SAWALL, LLP, 100 EAST WISCONSIN AVENUE, SUITE 1100, MILWAUKEE, WI, 53202

CLMN Number of Claims: 77

ECL Exemplary Claim: 1

DRWN 1 Drawing Page(s)

LN.CNT 979

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention discloses (20S)-1alpha-hydroxy-2alpha-methyl-19-nor-

vitamin D.sub.3 and (20S)-1 α -hydroxy-2 β -methyl-19-nor-vitamin D.sub.3 and pharmaceutical uses therefor. These compounds exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as an anti-cancer agent and for the treatment of skin diseases such as psoriasis as well as skin conditions such as wrinkles, slack skin, dry skin and insufficient sebum secretion. These compounds also have very significant calcemic activity and therefore may be used to treat immune disorders in humans as well as metabolic bone diseases such as osteoporosis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT **618104-20-4P**

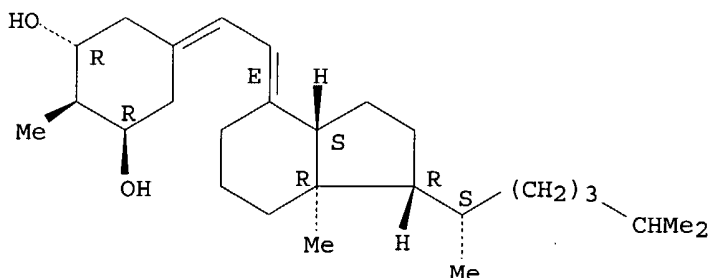
(nor-vitamin D3 derivs. and pharmaceutical uses)

RN 618104-20-4 USPATFULL

CN 1,3-Cyclohexanediol, 5-[(2E)-[(1R,3aS,7aR)-1-[(1S)-1,5-dimethylhexyl]octahydro-7a-methyl-4H-inden-4-ylidene]ethylidene]-2-methyl-, (1R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



IT **618104-21-5P**

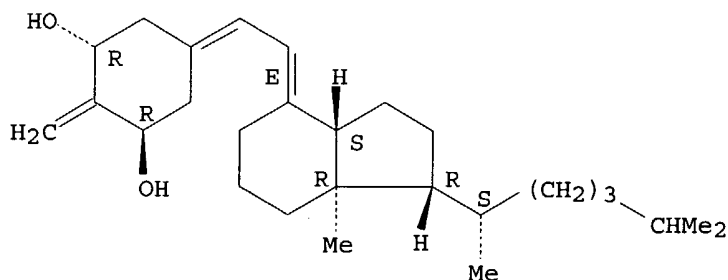
(nor-vitamin D3 derivs. and pharmaceutical uses)

RN 618104-21-5 USPATFULL

CN 1,3-Cyclohexanediol, 5-[(2E)-[(1R,3aS,7aR)-1-[(1S)-1,5-dimethylhexyl]octahydro-7a-methyl-4H-inden-4-ylidene]ethylidene]-2-methylene-, (1R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



L20 ANSWER 3 OF 7 USPATFULL on STN

AN 2004:197372 USPATFULL

TI (20S)-1 α -hydroxy-2 α -methyl and 2 β -methyl-19-nor-vitamin D3 and their uses

IN DeLuca, Hector F., Deerfield, WI, UNITED STATES
Sicinski, Rafal R., Warsaw, POLAND

Grzywacz, Pawel K., Madison, WI, UNITED STATES
 PA Wisconsin Alumni Research Foundation, Madison, WI (U.S. corporation)
 PI US 2004152678 A1 20040805
 AI US 2004-762911 A1 20040122 (10)
 RLI Division of Ser. No. US 2002-127180, filed on 22 Apr 2002, PENDING
 DT Utility
 FS APPLICATION
 LREP ANDRUS, SCEALES, STARKE & SAWALL, LLP, 100 EAST WISCONSIN AVENUE, SUITE
 1100, MILWAUKEE, WI, 53202
 CLMN Number of Claims: 77
 ECL Exemplary Claim: 1
 DRWN 1 Drawing Page(s)
 LN.CNT 977

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention discloses (20S)-1 α -hydroxy-2 α -methyl-19-nor-vitamin D.sub.3 and (20S)-1 α -hydroxy-2 β -methyl-19-nor-vitamin D.sub.3 and pharmaceutical uses therefor. These compounds exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as an anti-cancer agent and for the treatment of skin diseases such as psoriasis as well as skin conditions such as wrinkles, slack skin, dry skin and insufficient sebum secretion. These compounds also have very significant calcemic activity and therefore may be used to treat immune disorders in humans as well as metabolic bone diseases such as osteoporosis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT **618104-20-4P**

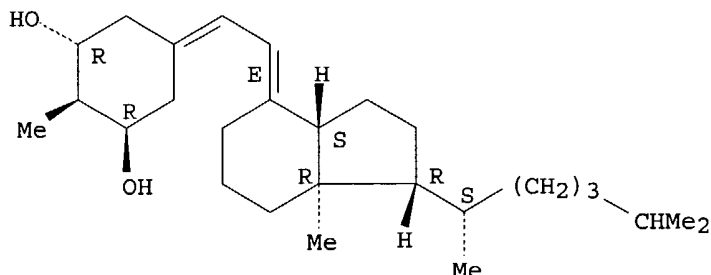
(nor-vitamin D3 derivs. and pharmaceutical uses)

RN 618104-20-4 USPATFULL

CN 1,3-Cyclohexanediol, 5-[(2E)-[(1R,3aS,7aR)-1-[(1S)-1,5-dimethylhexyl]octahydro-7a-methyl-4H-inden-4-ylidene]ethylidene]-2-methyl-, (1R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



IT **618104-21-5P**

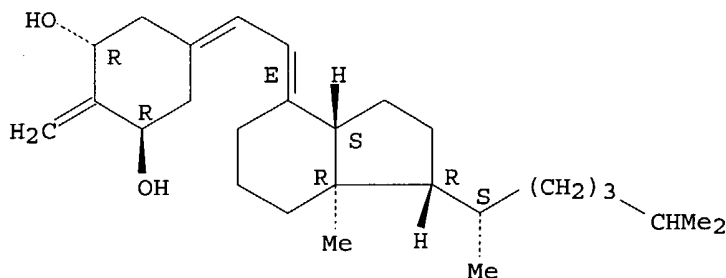
(nor-vitamin D3 derivs. and pharmaceutical uses)

RN 618104-21-5 USPATFULL

CN 1,3-Cyclohexanediol, 5-[(2E)-[(1R,3aS,7aR)-1-[(1S)-1,5-dimethylhexyl]octahydro-7a-methyl-4H-inden-4-ylidene]ethylidene]-2-methylene-, (1R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



L20 ANSWER 4 OF 7 USPATFULL on STN
 AN 2004:197371 USPATFULL
 TI (20S)-1 α -hydroxy-2 α -methyl and 2 β -methyl-19-nor-vitamin D3 and their uses
 IN DeLuca, Hector F., Deerfield, WI, UNITED STATES
 Sicinski, Rafal R., Warsaw, POLAND
 Grzywacz, Pawel K., Madison, WI, UNITED STATES
 PA Wisconsin Alumni Research Foundation, Madison, WI (U.S. corporation)
 PI US 2004152677 A1 20040805
 AI US 2004-762906 A1 20040122 (10)
 RLI Division of Ser. No. US 2002-127180, filed on 22 Apr 2002, PENDING
 DT Utility
 FS APPLICATION
 LREP ANDRUS, SCEALES, STARKE & SAWALL, LLP, 100 EAST WISCONSIN AVENUE, SUITE 1100, MILWAUKEE, WI, 53202
 CLMN Number of Claims: 77
 ECL Exemplary Claim: 1
 DRWN 1 Drawing Page(s)
 LN.CNT 980

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention discloses (20S)-1 α -hydroxy-2 α -methyl-19-nor-vitamin D.sub.3 and (20S)-1 α -hydroxy-2 β -methyl-19-nor-vitamin D.sub.3 and pharmaceutical uses therefor. These compounds exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as an anti-cancer agent and for the treatment of skin diseases such as psoriasis as well as skin conditions such as wrinkles, slack skin, dry skin and insufficient sebum secretion. These compounds also have very significant calcemic activity and therefore may be used to treat immune disorders in humans as well as metabolic bone diseases such as osteoporosis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 618104-20-4P

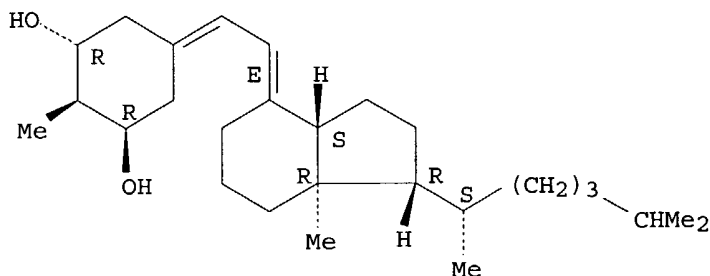
(nor-vitamin D3 derivs. and pharmaceutical uses)

RN 618104-20-4 USPATFULL

CN 1,3-Cyclohexanediol, 5-[(2E)-[(1R,3aS,7aR)-1-[(1S)-1,5-dimethylhexyl]octahydro-7a-methyl-4H-inden-4-ylidene]ethylidene]-2-methyl-, (1R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



IT 618104-21-5P

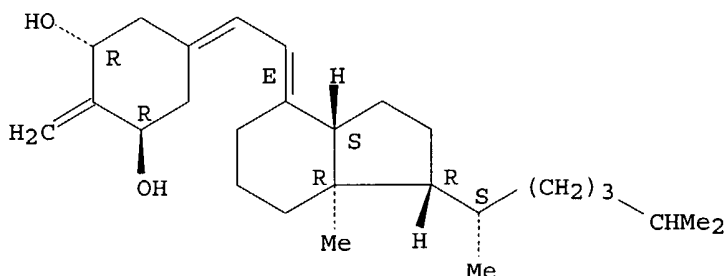
(nor-vitamin D3 derivs. and pharmaceutical uses)

RN 618104-21-5 USPTAFULL

CN 1,3-Cyclohexanediol, 5-[(2E)-[(1R,3aS,7aR)-1-[(1S)-1,5-dimethylhexyl]octahydro-7a-methyl-4H-inden-4-ylidene]ethylidene]-2-methylene-, (1R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



L20 ANSWER 5 OF 7 USPTAFULL on STN

AN 2004:197370 USPTAFULL

TI (20S)-1α-hydroxy-2α-methyl and 2β-methyl-19-nor-vitamin D3 and their uses

IN DeLuca, Hector F., Deerfield, WI, UNITED STATES

Sicinski, Rafal R., Warsaw, POLAND

Grzywacz, Pawel K., Madison, WI, UNITED STATES

PA Wisconsin Alumni Research Foundation, Madison, WI (U.S. corporation)

PI US 2004152676 A1 20040805

AI US 2004-762710 A1 20040122 (10)

RLI Division of Ser. No. US 2002-127180, filed on 22 Apr 2002, PENDING

DT Utility

FS APPLICATION

LREP ANDRUS, SCEALES, STARKE & SAWALL, LLP, 100 EAST WISCONSIN AVENUE, SUITE 1100, MILWAUKEE, WI, 53202

CLMN Number of Claims: 77

ECL Exemplary Claim: 1

DRWN 1 Drawing Page(s)

LN.CNT 978

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention discloses (20S)-1α-hydroxy-2α-methyl-19-nor-vitamin D.sub.3 and (20S)-1α-hydroxy-2β-methyl-19-nor-vitamin D.sub.3 and pharmaceutical uses therefor. These compounds exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as an anti-cancer agent and for the treatment of skin diseases such as psoriasis as well as skin conditions such as wrinkles, slack skin,

dry skin and insufficient sebum secretion. These compounds also have very significant calcemic activity and therefore may be used to treat immune disorders in humans as well as metabolic bone diseases such as osteoporosis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

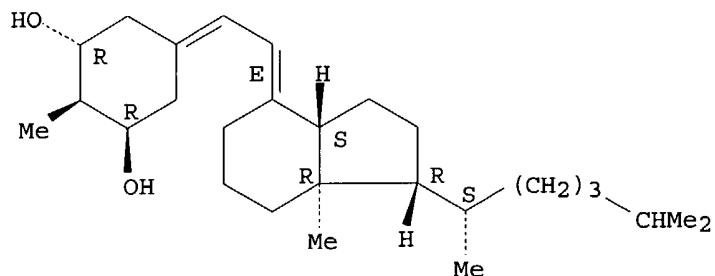
IT 618104-20-4P

(nor-vitamin D3 derivs. and pharmaceutical uses)

RN 618104-20-4 USPATFULL

CN 1,3-Cyclohexanediol, 5-[(2E)-[(1R,3aS,7aR)-1-[(1S)-1,5-dimethylhexyl]octahydro-7a-methyl-4H-inden-4-ylidene]ethylidene]-2-methyl-, (1R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



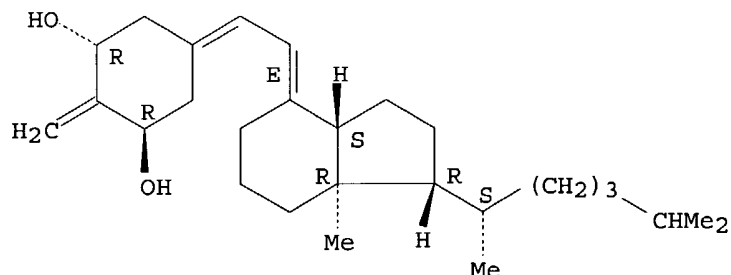
IT 618104-21-5P

(nor-vitamin D3 derivs. and pharmaceutical uses)

RN 618104-21-5 USPATFULL

CN 1,3-Cyclohexanediol, 5-[(2E)-[(1R,3aS,7aR)-1-[(1S)-1,5-dimethylhexyl]octahydro-7a-methyl-4H-inden-4-ylidene]ethylidene]-2-methylene-, (1R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L20 ANSWER 6 OF 7 USPATFULL on STN

AN 2004:197369 USPATFULL

TI (20S)-1alpha-hydroxy-2alpha-methyl and 2beta-methyl-19-nor-vitamin D3 and their uses

IN DeLuca, Hector F., Deerfield, WI, UNITED STATES

Sicinski, Rafal R., Warsaw, POLAND

Grzywacz, Pawel K., Madison, WI, UNITED STATES

PA Wisconsin Alumni Research Foundation, Madison, WI, UNITED STATES (U.S. corporation)

PI US 2004152675 A1 20040805

AI US 2004-762618 A1 20040122 (10)

RLI Division of Ser. No. US 2002-127180, filed on 22 Apr 2002, PENDING

DT Utility
 FS APPLICATION
 LREP ANDRUS, SCEALES, STARKE & SAWALL, LLP, 100 EAST WISCONSIN AVENUE, SUITE
 1100, MILWAUKEE, WI, 53202
 CLMN Number of Claims: 77
 ECL Exemplary Claim: 1
 DRWN 1 Drawing Page(s)
 LN.CNT 977

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention discloses (20S)-1 α -hydroxy-2 α -methyl-19-nor-vitamin D.sub.3 and (20S)-1 α -hydroxy-2 β -methyl-19-nor-vitamin D.sub.3 and pharmaceutical uses therefor. These compounds exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as an anti-cancer agent and for the treatment of skin diseases such as psoriasis as well as skin conditions such as wrinkles, slack skin, dry skin and insufficient sebum secretion. These compounds also have very significant calcemic activity and therefore may be used to treat immune disorders in humans as well as metabolic bone diseases such as osteoporosis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

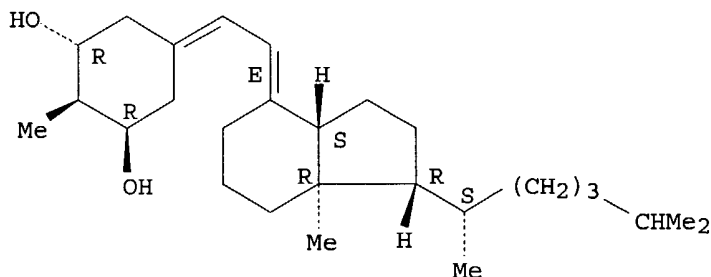
IT 618104-20-4P

(nor-vitamin D3 derivs. and pharmaceutical uses)

RN 618104-20-4 USPATFULL

CN 1,3-Cyclohexanediol, 5-[(2E)-[(1R,3aS,7aR)-1-[(1S)-1,5-dimethylhexyl]octahydro-7a-methyl-4H-inden-4-ylidene]ethylidene]-2-methyl-, (1R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.



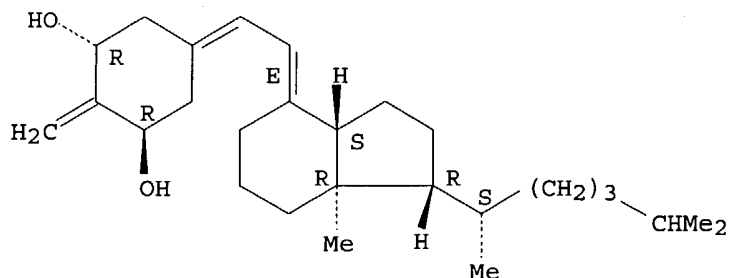
IT 618104-21-5P

(nor-vitamin D3 derivs. and pharmaceutical uses)

RN 618104-21-5 USPATFULL

CN 1,3-Cyclohexanediol, 5-[(2E)-[(1R,3aS,7aR)-1-[(1S)-1,5-dimethylhexyl]octahydro-7a-methyl-4H-inden-4-ylidene]ethylidene]-2-methylene-, (1R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.



L20 ANSWER 7 OF 7 USPATFULL on STN

AN 2003:289123 USPATFULL

TI (20S) 1alpha-hydroxy-2alpha-methyl and 2beta-methyl-19-nor-vitamin D3 and their uses

IN DeLuca, Hector F., Deerfield, WI, UNITED STATES

Sicinski, Rafal R., Warsaw, POLAND

Grzywacz, Pawel K., Madison, WI, UNITED STATES

PI US 2003203882 A1 20031030

AI US 2002-127180 A1 20020422 (10)

DT Utility

FS APPLICATION

LREP KINNEY & LANGE, P.A., THE KINNEY & LANGE BUILDING, 312 SOUTH THIRD STREET, MINNEAPOLIS, MN, 55415-1002

CLMN Number of Claims: 77

ECL Exemplary Claim: 1

DRWN 1 Drawing Page(s)

LN.CNT 979

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention discloses (20S)-1 α -hydroxy-2 α -methyl-19-nor-vitamin D.sub.3 and (20S)-1 α -hydroxy-2 β -methyl-19-nor-vitamin D.sub.3 and pharmaceutical uses therefor. These compounds exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as an anti-cancer agent and for the treatment of skin diseases such as psoriasis as well as skin conditions such as wrinkles, slack skin, dry skin and insufficient sebum secretion. These compounds also have very significant calcemic activity and therefore may be used to treat immune disorders in humans as well as metabolic bone diseases such as osteoporosis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 618104-20-4P

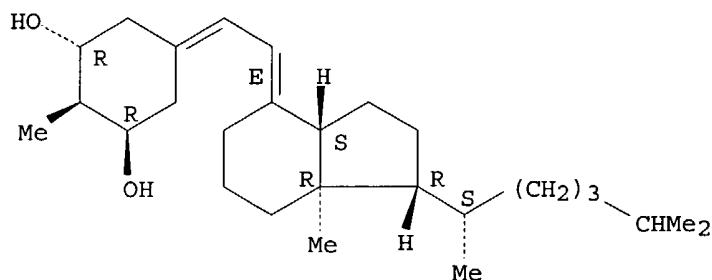
(nor-vitamin D3 derivs. and pharmaceutical uses)

RN 618104-20-4 USPATFULL

CN 1,3-Cyclohexanediol, 5-[(2E)-[(1R,3aS,7aR)-1-[(1S)-1,5-dimethylhexyl]octahydro-7a-methyl-4H-inden-4-ylidene]ethylidene]-2-methyl-, (1R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



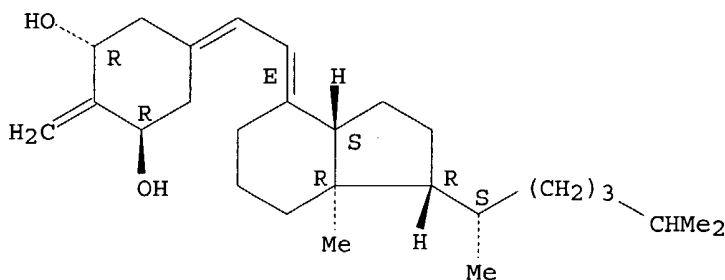
IT 618104-21-5P

(nor-vitamin D3 derivs. and pharmaceutical uses)

RN 618104-21-5 USPATFULL

CN 1,3-Cyclohexanediol, 5-[(2E)-[(1R,3aS,7aR)-1-[(1S)-1,5-dimethylhexyl]octahydro-7a-methyl-4H-inden-4-ylidene]ethylidene]-2-methylene-, (1R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



=> => fil reg

FILE 'REGISTRY' ENTERED AT 10:15:55 ON 25 AUG 2004

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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 24 AUG 2004 HIGHEST RN 732209-96-0

DICTIONARY FILE UPDATES: 24 AUG 2004 HIGHEST RN 732209-96-0

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

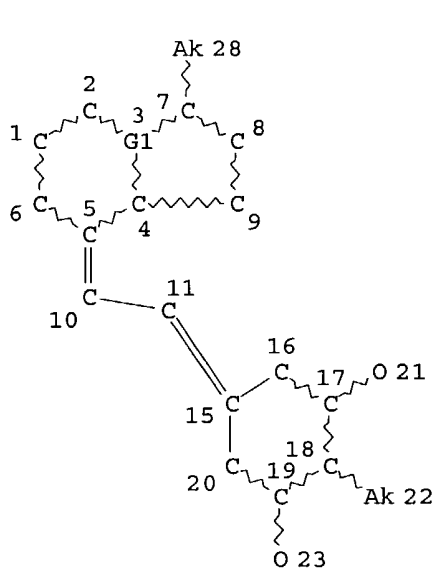
Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
<http://www.cas.org/ONLINE/DBSS/registryss.html>

=> d sta que 125

L23 STR



27
Ak
|
C
@25

VAR G1=C/25

NODE ATTRIBUTES:

CONNECT IS M1 RC AT 21

CONNECT IS M1 RC AT 23

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 23

STEREO ATTRIBUTES: NONE

L25 8 SEA FILE=REGISTRY CSS FUL L23

100.0% PROCESSED 7356 ITERATIONS

8 ANSWERS

SEARCH TIME: 00.00.01

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(FILE 'HOME' ENTERED AT 10:03:09 ON 25 AUG 2004)

SET COST OFF

FILE 'HCAPLUS' ENTERED AT 10:03:21 ON 25 AUG 2004

L1 1 S US20040152675/PN

SEL RN

FILE 'REGISTRY' ENTERED AT 10:03:39 ON 25 AUG 2004

L2 17 S E1-E17

L3 1 S L2 AND C27H46O2

E C27H46O2/MF

L4 19 S E3 AND C5-C6/ES AND C6/ES AND 3/NR NOT 46.150.18/RID

SEL RN L3

L5 0 S E1/CRN

FILE 'HCAOLD' ENTERED AT 10:06:05 ON 25 AUG 2004

L6 0 S L3

FILE 'HCAPLUS' ENTERED AT 10:06:07 ON 25 AUG 2004

L7 1 S L3

L8 FILE 'USPATFULL, USPAT2' ENTERED AT 10:06:11 ON 25 AUG 2004
7 S L3

FILE 'REGISTRY' ENTERED AT 10:06:25 ON 25 AUG 2004

FILE 'HCAPLUS' ENTERED AT 10:06:31 ON 25 AUG 2004

FILE 'USPATFULL, USPAT2' ENTERED AT 10:06:40 ON 25 AUG 2004

FILE 'REGISTRY' ENTERED AT 10:07:13 ON 25 AUG 2004

L9 8 S L2 AND C5-C6/ES AND C6/ES NOT L3
L10 3 S L9 NOT 46.150.18/RID
L11 2 S L10 NOT SI/ELS
L12 1 S L11 NOT 50-14-6
L13 2 S L3,L12
E C27H44O2/MF
L14 117 S E3 AND C5-C6/ES AND C6/ES AND 3/NR NOT 46.150.18/RID
L15 1 S L14 AND 1 3 CYCLOHEXANEDIOL
L16 2 S L14 AND METHYLENE
SEL RN L12
L17 0 S E1/CRN

FILE 'HCAOLD' ENTERED AT 10:09:36 ON 25 AUG 2004

L18 0 S L13

FILE 'HCAPLUS' ENTERED AT 10:09:37 ON 25 AUG 2004

L19 1 S L13

FILE 'USPATFULL, USPAT2' ENTERED AT 10:09:42 ON 25 AUG 2004

L20 7 S L13

FILE 'REGISTRY' ENTERED AT 10:09:50 ON 25 AUG 2004

FILE 'HCAPLUS' ENTERED AT 10:09:58 ON 25 AUG 2004

FILE 'USPATFULL, USPAT2' ENTERED AT 10:10:13 ON 25 AUG 2004

FILE 'REGISTRY' ENTERED AT 10:11:21 ON 25 AUG 2004

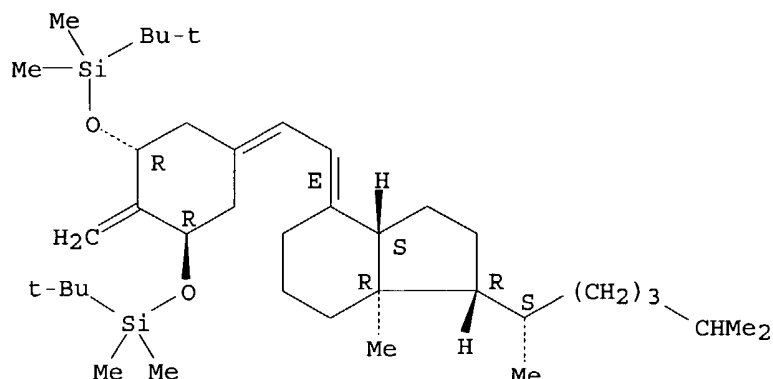
L21 STR
L22 0 S L21 CSS
L23 STR L21
L24 1 S L23 CSS
L25 8 S L23 CSS FUL
SAV L25 QAZI762/A
L26 6 S L25 NOT L13

FILE 'REGISTRY' ENTERED AT 10:15:55 ON 25 AUG 2004

=> d ide can tot l26

L26 ANSWER 1 OF 6 REGISTRY COPYRIGHT 2004 ACS on STN
RN 618104-22-6 REGISTRY
CN Silane, [[(1 α ,3 β ,7E,20S)-2-methylene-19-nor-9,10-secocholesta-5,7,10(19)-triene-1,3-diyl]bis(oxy)]bis(1,1-dimethylethyl)dimethyl- (9CI)
(CA INDEX NAME)
FS STEREOSEARCH
MF C39 H72 O2 Si2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL
DT.CA Caplus document type: Patent
RL.P Roles from patents: PREP (Preparation); RACT (Reactant or reagent)

Absolute stereochemistry.
Double bond geometry as shown.



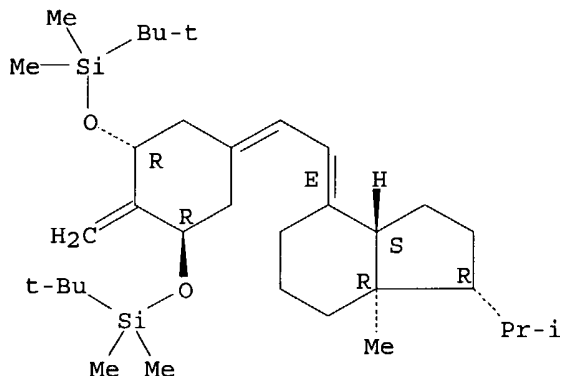
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:345953

L26 ANSWER 2 OF 6 REGISTRY COPYRIGHT 2004 ACS on STN
RN 610304-71-7 REGISTRY
CN Silane, [[(1R,3R)-2-methylene-5-[(2E)-[(1R,3aS,7aR)-octahydro-7a-methyl-1-(1-methylethyl)-4H-inden-4-ylidene]ethylidene]-1,3-cyclohexanediyl]bis(oxy)]bis[(1,1-dimethylethyl)dimethyl- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C34 H62 O2 Si2
SR CA
LC STN Files: CA, CAPLUS, CASREACT, USPAT2, USPATFULL
DT.CA Caplus document type: Patent
RL.P Roles from patents: PREP (Preparation); RACT (Reactant or reagent)

Absolute stereochemistry.
Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

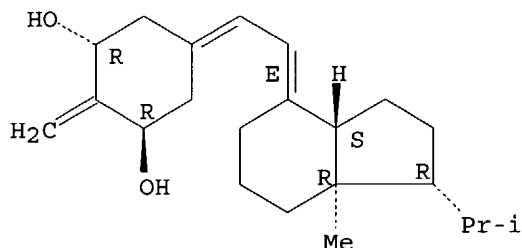
1 REFERENCES IN FILE CA (1907 TO DATE)

1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:307926

L26 ANSWER 3 OF 6 REGISTRY COPYRIGHT 2004 ACS on STN
 RN 524067-22-9 REGISTRY
 CN 1,3-Cyclohexanediol, 2-methylene-5-[(2E)-[(1R,3aS,7aR)-octahydro-7a-methyl-1-(1-methylethyl)-4H-inden-4-ylidene]ethylidene]-, (1R,3R)- (9CI) (CA INDEX NAME)
 FS STEREOSEARCH
 MF C22 H34 O2
 SR CA
 LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER, USPAT2, USPATFULL
 DT.CA Caplus document type: Journal; Patent
 RL.P Roles from patents: BIOL (Biological study); PREP (Preparation)
 RL.NP Roles from non-patents: BIOL (Biological study); PRP (Properties)

Absolute stereochemistry.
 Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

4 REFERENCES IN FILE CA (1907 TO DATE)
 4 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 141:82860

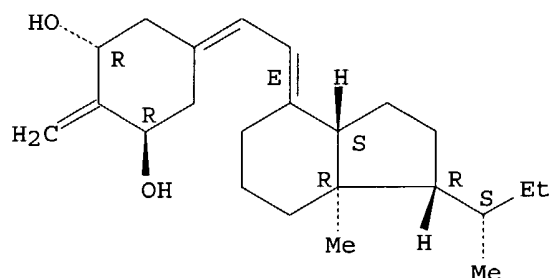
REFERENCE 2: 139:317525

REFERENCE 3: 139:307926

REFERENCE 4: 138:363223

L26 ANSWER 4 OF 6 REGISTRY COPYRIGHT 2004 ACS on STN
 RN 524067-21-8 REGISTRY
 CN 1,3-Cyclohexanediol, 2-methylene-5-[(2E)-[(1R,3aS,7aR)-octahydro-7a-methyl-1-[(1S)-1-methylpropyl]-4H-inden-4-ylidene]ethylidene]-, (1R,3R)- (9CI) (CA INDEX NAME)
 OTHER NAMES:
 CN (20S)-1 α -Hydroxy-2-methylene-19-norbishomopregnacalciferol
 CN Becocalcidiol
 CN QRX 101
 FS STEREOSEARCH
 MF C23 H36 O2
 SR CA
 LC STN Files: CA, CAPLUS, PROUSDDR, TOXCENTER, USPAT2, USPATFULL
 DT.CA Caplus document type: Journal; Patent
 RL.P Roles from patents: BIOL (Biological study); PRP (Properties); USES (Uses)
 RL.NP Roles from non-patents: BIOL (Biological study); PRP (Properties)

Absolute stereochemistry.
Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

4 REFERENCES IN FILE CA (1907 TO DATE)
4 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 141:82860

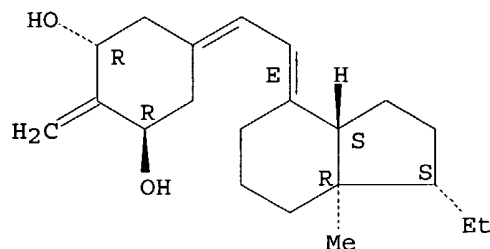
REFERENCE 2: 140:386155

REFERENCE 3: 139:53211

REFERENCE 4: 138:363223

L26 ANSWER 5 OF 6 REGISTRY COPYRIGHT 2004 ACS on STN
RN 524067-20-7 REGISTRY
CN 1,3-Cyclohexanediol, 5-[(2E)-[(1S,3aS,7aR)-1-ethyloctahydro-7a-methyl-4H-inden-4-ylidene]ethylidene]-2-methylene-, (1R,3R)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C21 H32 O2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL
DT.CA Caplus document type: Journal; Patent
RL.P Roles from patents: BIOL (Biological study); USES (Uses)
RL.NP Roles from non-patents: BIOL (Biological study); PRP (Properties)

Absolute stereochemistry.
Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 141:82860

REFERENCE 2: 138:363223

L26 ANSWER 6 OF 6 REGISTRY COPYRIGHT 2004 ACS on STN

RN 403647-27-8 REGISTRY

CN 1,3-Cyclohexanediol, 2-methylene-5-[(2E)-[(3aS,7aR)-octahydro-7a-methyl-1-(1-methylethyl)-4H-inden-4-ylidene]ethylidene]-, (1R,3R)- (9CI) (CA INDEX NAME)

FS STEREOSEARCH

MF C22 H34 O2

SR CA

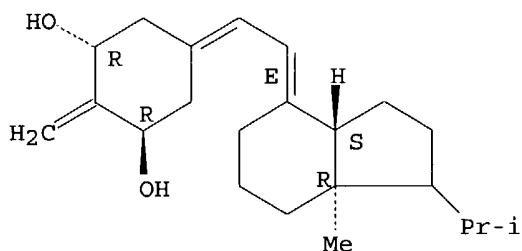
LC STN Files: CA, CAPLUS, TOXCENTER, USPAT2, USPATFULL

DT.CA Caplus document type: Patent

RL.P Roles from patents: BIOL (Biological study); USES (Uses)

Absolute stereochemistry.

Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1907 TO DATE)

2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 136:335278

REFERENCE 2: 136:226818

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(FILE 'HOME' ENTERED AT 10:20:44 ON 25 AUG 2004)

SET COST OFF

FILE 'REGISTRY' ENTERED AT 10:20:50 ON 25 AUG 2004

ACT QAZI762/A

L1 STR

L2 8 SEA FILE=REGISTRY CSS FUL L1

L3 6 S L2 NOT (618104-21-5 OR 618104-20-4)

FILE 'HCAOLD' ENTERED AT 10:21:16 ON 25 AUG 2004

L4 0 S L3

FILE 'HCAPLUS' ENTERED AT 10:21:18 ON 25 AUG 2004

L5 9 S L3

L6 6 S L5 AND (PD<=20020422 OR PRD<=20020422 OR AD<=20020422)

L7 9 S L5 AND (DELUCA ? OR DE LUCA ? OR SICINSKI ? OR GRZYWACZ ?)/AU

L8 9 S L5-L7

FILE 'USPATFULL, USPAT2' ENTERED AT 10:22:34 ON 25 AUG 2004

L9 18 S L3

L10 18 S L9 AND (DELUCA ? OR DE LUCA ? OR SICINSKI ? OR GRZYWACZ ?)/A

=> fil hcaplus

FILE 'HCAPLUS' ENTERED AT 10:23:03 ON 25 AUG 2004

USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.

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FILE COVERS 1907 - 25 Aug 2004 VOL 141 ISS 9

FILE LAST UPDATED: 24 Aug 2004 (20040824/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d 18 all hitstr tot

L8 ANSWER 1 OF 9 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2004:413892 HCAPLUS

DN 141:82860

ED Entered STN: 21 May 2004

TI Biologically active noncalcemic analogs of 1 α ,25-dihydroxyvitamin D with an abbreviated side chain containing no hydroxyl

AU Plum, Lori A.; Prahl, Jean M.; Ma, Xiaohong; **Sicinski, Rafal R.**;

Gowlugari, Sumithra; Clagett-Dame, Margaret; **DeLuca, Hector F.**

CS Department of Biochemistry, University of Wisconsin, Madison, WI, 53706, USA

SO Proceedings of the National Academy of Sciences of the United States of America (2004), 101(18), 6900-6904

CODEN: PNASA6; ISSN: 0027-8424

PB National Academy of Sciences

DT Journal

LA English

CC 2-10 (Mammalian Hormones)

AB Since the discovery of the active metabolite of vitamin D, i.e., 1 α ,25-dihydroxyvitamin D₃, there has been a continuous effort to synthesize analogs able to carry out many of the functions of the native hormone without raising serum calcium concentration The present report provides

a series of previously undescribed analogs wherein this goal is realized. The authors have prepared 2-methylene-19-nor-1 α -hydroxyvitamin D analogs of 1,25-(OH)₂D₃ that possess only two to four carbons of the side chain without a hydroxyl thereon. Compared to 1,25-(OH)₂D₃, these analogs are slightly less active in binding to the vitamin D receptor, in causing HL-60 differentiation, and are slightly less active in in vitro transcription assays using the 24-hydroxylase promoter attached to a luciferase reporter gene. Of considerable importance is that these analogs, given to rats at daily doses of up to 70 μ g/kg of body weight per day, are either unable or only slightly able to raise serum calcium concentration

but are nevertheless able to suppress parathyroid hormone levels in plasma up to 100% and induce 24-hydroxylase mRNA in skin. Because of their

ability to act in vivo without raising serum calcium levels, they may be of considerable interest for the systemic treatment of diseases such as psoriasis, cancer, and secondary hyperparathyroidism of renal failure, where a rise in serum calcium is undesirable.

- ST dihydroxyvitamin D3 analog calcium blood rat
IT mRNA
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(24-hydroxylase; biol. active noncalcemic analogs of
1 α ,25-dihydroxyvitamin D with an abbreviated side chain containing no
hydroxyl as evaluated in rat, HL-60 and osteosarcoma 17/2.8 cells)
- IT Blood serum
Bone
Cell differentiation
Human
(biol. active noncalcemic analogs of 1 α ,25-dihydroxyvitamin D
with an abbreviated side chain containing no hydroxyl as evaluated in rat,
HL-60 and osteosarcoma 17/2.8 cells)
- IT Vitamin D receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(biol. active noncalcemic analogs of 1 α ,25-dihydroxyvitamin D
with an abbreviated side chain containing no hydroxyl as evaluated in rat,
HL-60 and osteosarcoma 17/2.8 cells)
- IT Skin
(keratinocyte, 24-hydroxylase mRNA; biol. active noncalcemic analogs of
1 α ,25-dihydroxyvitamin D with an abbreviated side chain containing no
hydroxyl as evaluated in rat, HL-60 and osteosarcoma 17/2.8 cells)
- IT 3352-57-6, Hydroxyl, biological studies 7440-70-2, Calcium, biological
studies 9002-64-6, Parathyroid hormone 32222-06-3,
1 α ,25-Dihydroxyvitamin D3 67272-34-8, Calcitriol 24-hydroxylase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(biol. active noncalcemic analogs of 1 α ,25-dihydroxyvitamin D
with an abbreviated side chain containing no hydroxyl as evaluated in rat,
HL-60 and osteosarcoma 17/2.8 cells)
- IT 524067-20-7 524067-21-8 524067-22-9
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL
(Biological study)
(biol. active noncalcemic analogs of 1 α ,25-dihydroxyvitamin D
with an abbreviated side chain containing no hydroxyl as evaluated in rat,
HL-60 and osteosarcoma 17/2.8 cells)

RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

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IT 524067-20-7 524067-21-8 524067-22-9
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL

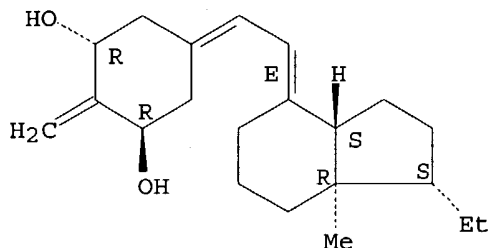
(Biological study)

(biol. active noncalcemic analogs of 1 α ,25-dihydroxyvitamin D
with an abbreviated side chain containing no hydroxyl as evaluated in rat,
HL-60 and osteosarcoma 17/2.8 cells)

RN 524067-20-7 HCAPLUS

CN 1,3-Cyclohexanediol, 5-[(2E)-[(1S,3aS,7aR)-1-ethyloctahydro-7a-methyl-4H-inden-4-ylidene]ethylidene]-2-methylene-, (1R,3R)- (9CI) (CA INDEX NAME)

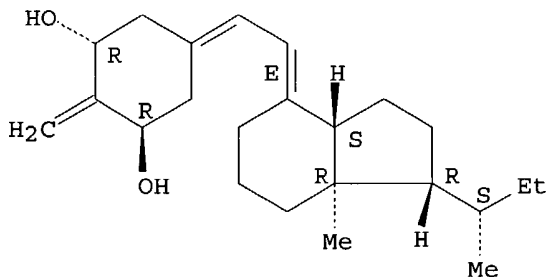
Absolute stereochemistry.
Double bond geometry as shown.



RN 524067-21-8 HCAPLUS

CN 1,3-Cyclohexanediol, 2-methylene-5-[(2E)-[(1R,3aS,7aR)-octahydro-7a-methyl-1-[(1S)-1-methylpropyl]-4H-inden-4-ylidene]ethylidene]-, (1R,3R)- (9CI) (CA INDEX NAME)

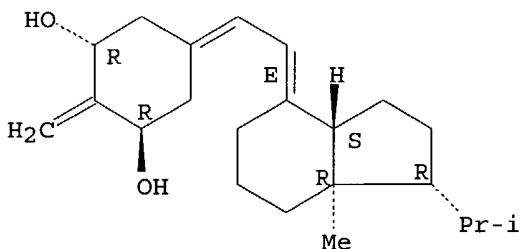
Absolute stereochemistry.
Double bond geometry as shown.



RN 524067-22-9 HCAPLUS

CN 1,3-Cyclohexanediol, 2-methylene-5-[(2E)-[(1R,3aS,7aR)-octahydro-7a-methyl-1-(1-methylethyl)-4H-inden-4-ylidene]ethylidene]-, (1R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



AN 2004:191311 HCAPLUS
DN 140:386155
ED Entered STN: 10 Mar 2004
TI Molecular structure of rat vitamin D receptor ligand binding domain
complexed with 2-carbon-substituted vitamin D3 hormone analogs and a
LXXLL-containing coactivator peptide
AU Vanhooke, Janeen L.; Benning, Matthew M.; Bauer, Cary B.; Pike, J. Wesley;
DeLuca, Hector F.
CS Department of Biochemistry, University of Wisconsin, Madison, WI, 53706,
USA
SO Biochemistry (2004), 43(14), 4101-4110
CODEN: BICHAW; ISSN: 0006-2960
PB American Chemical Society
DT Journal
LA English
CC 2-2 (Mammalian Hormones)
AB The authors have determined the crystal structures of the ligand binding domain
(LBD) of the rat vitamin D receptor in ternary complexes with a synthetic
LXXLL-containing peptide and the following four ligands: 1 α ,25-
dihydroxyvitamin D3; 2-methylene-19-nor-(20S)-1 α ,25-dihydroxyvitamin
D3 (2MD); 1 α -hydroxy-2-methylene-19-nor-(20S)-
bishomopregnacalciferol (2Mbisp), and 2 α -methyl-19-nor-1 α ,25-
dihydroxyvitamin D3 (2AM20R). The conformation of the LBD is identical in
each complex. Binding of the 2-carbon-modified analogs does not change
the positions of the amino acids in the ligand binding site and has no
effect on the interactions in the coactivator binding pocket. The CD ring
of the superpotent analog, 2MD, is tilted within the binding site relative
to the other ligands in this study and to (20S)-1 α ,25-
dihydroxyvitamin D3. The aliphatic side chain of 2MD follows a different
path within the binding site; nevertheless, the 25-hydroxyl group at the
end of the chain occupies the same position as that of the natural ligand,
and the hydrogen bonds with histidines 301 and 393 are maintained. 2Mbisp
binds to the receptor despite the absence of the 25-hydroxyl group. A
water mol. is observed between His 301 and His 393 in this structure, and it
preserves the orientation of the histidines in the binding site. Although
the α -chair conformer is highly favored in solution for the A ring of
2AM20R, the crystal structures demonstrate that this ring assumes the
 β -chair conformation in all cases, and the 1 α -hydroxyl group is
equatorial. The peptide folds as a helix and is anchored through hydrogen
bonds to a surface groove formed by helices 3, 4, and 12. Electrostatic
and hydrophobic interactions between the peptide and the LBD stabilize the
active receptor conformation. This stabilization appears necessary for
crystal growth.
ST vitamin D3 receptor protein motif peptide complex crystal structure
IT Transcription factors
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL
(Biological study)
(DRIP 205; mol. structure of rat vitamin D receptor ligand binding
domain complexed with 2-carbon-substituted vitamin D3 hormone analogs
and LXXLL-containing coactivator peptide)
IT Bond length
Hydrogen bond
Hydroxyl group
Protein motifs
(mol. structure of rat vitamin D receptor ligand binding domain
complexed with 2-carbon-substituted vitamin D3 hormone analogs and
LXXLL-containing coactivator peptide)
IT Vitamin D receptors
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL
(Biological study)
(mol. structure of rat vitamin D receptor ligand binding domain
complexed with 2-carbon-substituted vitamin D3 hormone analogs and
LXXLL-containing coactivator peptide)

IT Helix (conformation)
(protein; mol. structure of rat vitamin D receptor ligand binding domain complexed with 2-carbon-substituted vitamin D3 hormone analogs and LXXLL-containing coactivator peptide)

IT Bond angle
(torsional; mol. structure of rat vitamin D receptor ligand binding domain complexed with 2-carbon-substituted vitamin D3 hormone analogs and LXXLL-containing coactivator peptide)

IT 32222-06-3, 1 α ,25-Dihydroxyvitamin D3 131875-08-6, KH1060
134523-84-5, MC1288 213250-70-5 217446-51-0 **524067-21-8**
685835-65-8
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(mol. structure of rat vitamin D receptor ligand binding domain complexed with 2-carbon-substituted vitamin D3 hormone analogs and LXXLL-containing coactivator peptide)

IT 71-00-1, L-Histidine, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(residues 301 and 393; mol. structure of rat vitamin D receptor ligand binding domain complexed with 2-carbon-substituted vitamin D3 hormone analogs and LXXLL-containing coactivator peptide)

RE.CNT 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD

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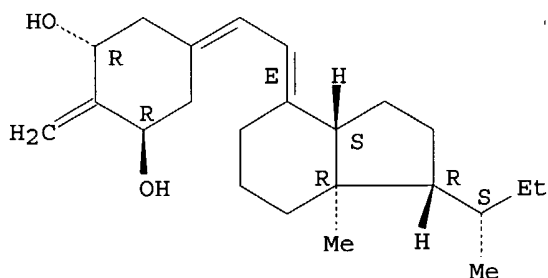
IT 524067-21-8

RL: BSU (Biological study, unclassified); PRP (Properties); BIOL
 (Biological study)
 (mol. structure of rat vitamin D receptor ligand binding domain
 complexed with 2-carbon-substituted vitamin D3 hormone analogs and
 LXXLL-containing coactivator peptide)

RN 524067-21-8 HCAPLUS

CN 1,3-Cyclohexanediol, 2-methylene-5-[(2E)-[(1R,3aS,7aR)-octahydro-7a-methyl-
 1-[(1S)-1-methylpropyl]-4H-inden-4-ylidene]ethylidene]-, (1R,3R)- (9CI)
 (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.



L8 ANSWER 3 OF 9 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2003:855808 HCAPLUS

DN 139:345953

ED Entered STN: 31 Oct 2003

TI (20S)-1 α -Hydroxy-2 α -methyl--19-nor-vitamin D3 and
 (20S)-1 α -hydroxy-2 β -methyl--19-nor-vitamin D3, and
 pharmaceutical uses

IN Deluca, Hector F.; Sicinski, Rafal R.; Grzywacz,
 Pawel K.

PA Wisconsin Alumni Research Foundation, USA

SO PCT Int. Appl., 44 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM A61K031-593

ICS A61P017-06; A61P019-10; A61P035-00; A61P037-06

CC 1-12 (Pharmacology)

Section cross-reference(s): 32, 63

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003088977	A1	20031030	WO 2003-US8423	20030320 <--
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	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,				
	CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,				
	GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,				

LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
 PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA,
 UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
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 CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC,
 NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ,
 GW, ML, MR, NE, SN, TD, TG

US 2003203882	A1	20031030	US 2002-127180	20020422 <--
US 2004152675	A1	20040805	US 2004-762618	20040122 <--
US 2004152676	A1	20040805	US 2004-762710	20040122 <--
US 2004152677	A1	20040805	US 2004-762906	20040122 <--
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US 2004152680	A1	20040805	US 2004-763029	20040122 <--
PRAI US 2002-127180	A	20020422	<--	

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
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WO 2003088977	ICM	A61K031-593
	ICS	A61P017-06; A61P019-10; A61P035-00; A61P037-06

AB The invention discloses (20S)-1 α -hydroxy-2 α -methyl-19-nor-vitamin D3 and (20S)-1 α -hydroxy-2 β -methyl-19-nor-vitamin D3 and pharmaceutical uses therefor. These compds. exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte, thus evidencing use as an anticancer agent and for the treatment of skin diseases, e.g. psoriasis, as well as skin conditions such as wrinkles, slack skin, dry skin and insufficient sebum secretion. These compds. also have very significant calcemic activity and therefore may be used to treat immune disorders in humans as well as metabolic bone diseases, e.g. osteoporosis. Compound preparation is described.

ST norvitamin D3 deriv prepn therapeutic; antitumor skin condition therapy
 norvitamin D3 deriv; immune disease osteoporosis norvitamin D3 deriv;
 metabolic bone disease norvitamin D3 deriv

IT Animal cell line
 (HL-60; nor-vitamin D3 derivs. and pharmaceutical uses)

IT Bone
 (bone mass increase; nor-vitamin D3 derivs. and pharmaceutical uses)

IT Biological transport
 (calcium; nor-vitamin D3 derivs. and pharmaceutical uses)

IT Intestine, neoplasm
 (colon; nor-vitamin D3 derivs. and pharmaceutical uses)

IT Drugs
 (gastrointestinal; nor-vitamin D3 derivs. and pharmaceutical uses)

IT Transplant and Transplantation
 (host-vs.-graft reaction; nor-vitamin D3 derivs. and pharmaceutical uses)

IT Hydration, physiological
 (inadequate dermal hydration; nor-vitamin D3 derivs. and pharmaceutical uses)

IT Cell differentiation
 (inducers; nor-vitamin D3 derivs. and pharmaceutical uses)

IT Intestine, disease
 (inflammatory; nor-vitamin D3 derivs. and pharmaceutical uses)

IT Sebum
 (insufficient secretion; nor-vitamin D3 derivs. and pharmaceutical uses)

IT Osteoporosis
 (low bone turnover osteoporosis; nor-vitamin D3 derivs. and pharmaceutical uses)

IT Anti-inflammatory agents
 Antiasthmatics
 Antidiabetic agents

Antirheumatic agents
 Antitumor agents
 Asthma
 Autoimmune disease
 Cell differentiation
 Diabetes mellitus
 Human
 Inflammation
 Leukemia
 Lupus erythematosus
 Mammary gland, neoplasm
 Monocyte
 Multiple sclerosis
 Osteomalacia
 Prostate gland, neoplasm
 Psoriasis
 Rheumatoid arthritis
 Transplant rejection
 (nor-vitamin D3 derivs. and pharmaceutical uses)
 IT Vitamin D receptors
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (nor-vitamin D3 derivs. and pharmaceutical uses)
 IT Drug delivery systems
 (oral; nor-vitamin D3 derivs. and pharmaceutical uses)
 IT Bone, disease
 (osteopenia; nor-vitamin D3 derivs. and pharmaceutical uses)
 IT Drug delivery systems
 (parenterals; nor-vitamin D3 derivs. and pharmaceutical uses)
 IT Osteoporosis
 (postmenopausal; nor-vitamin D3 derivs. and pharmaceutical uses)
 IT Myelocyte
 (promyelocyte; nor-vitamin D3 derivs. and pharmaceutical uses)
 IT Aging, animal
 (senile osteoporosis; nor-vitamin D3 derivs. and pharmaceutical uses)
 IT Steroids, biological studies
 RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
 (steroid-induced osteoporosis; nor-vitamin D3 derivs. and pharmaceutical uses)
 IT Drug delivery systems
 (topical; nor-vitamin D3 derivs. and pharmaceutical uses)
 IT Drug delivery systems
 (transdermal; nor-vitamin D3 derivs. and pharmaceutical uses)
 IT Skin
 (wrinkles and other conditions; nor-vitamin D3 derivs. and pharmaceutical uses)
 IT 7440-70-2, Calcium, biological studies
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (nor-vitamin D3 derivs. and pharmaceutical uses)
 IT 618104-20-4P
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (nor-vitamin D3 derivs. and pharmaceutical uses)
 IT 50-14-6, Vitamin D2 98-59-9, p-Toluenesulfonyl chloride 98-88-4, Benzoyl chloride 4237-74-5 213250-64-7
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (nor-vitamin D3 derivs. and pharmaceutical uses)
 IT 64190-52-9P 66774-70-7P 66774-71-8P 115527-12-3P 145354-28-5P 235108-01-7P 235108-02-8P 618104-21-5P **618104-22-6P** 618879-43-9P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (nor-vitamin D3 derivs. and pharmaceutical uses)

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

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IT 618104-22-6P

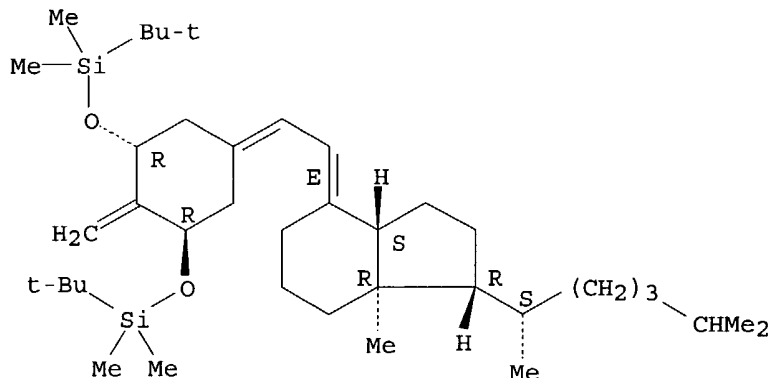
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(nor-vitamin D3 derivs. and pharmaceutical uses)

RN 618104-22-6 HCAPLUS

CN Silane, [[(1 α ,3 β ,7E,20S)-2-methylene-19-nor-9,10-secocholesta-
5,7,10(19)-triene-1,3-diyl]bis(oxy)]bis(1,1-dimethylethyl)dimethyl- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



L8 ANSWER 4 OF 9 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2003:796312 HCAPLUS

DN 139:307926

ED Entered STN: 10 Oct 2003

TI Process for preparing 1 α -hydroxy-2-methylene-19-nor-
homopregnacalciferol from vitamin D2

IN Deluca, Hector F.; Gowlugari, Sumithra; Sicinski, Rafal
R.

PA Wisconsin Alumni Research Foundation, USA

SO U.S. Pat. Appl. Publ., 9 pp.

CODEN: USXXCO

DT Patent

LA English

IC ICM A61K031-59

ICS C07C401-00

NCL 514167000; 552653000

CC 32-7 (Steroids)

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2003191095	A1	20031009	US 2003-397135	20030326 <--
	US 6774251	B2	20040810		
	WO 2003084925	A1	20031016	WO 2003-US9186	20030326 <--
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA,				

UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
 CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC,
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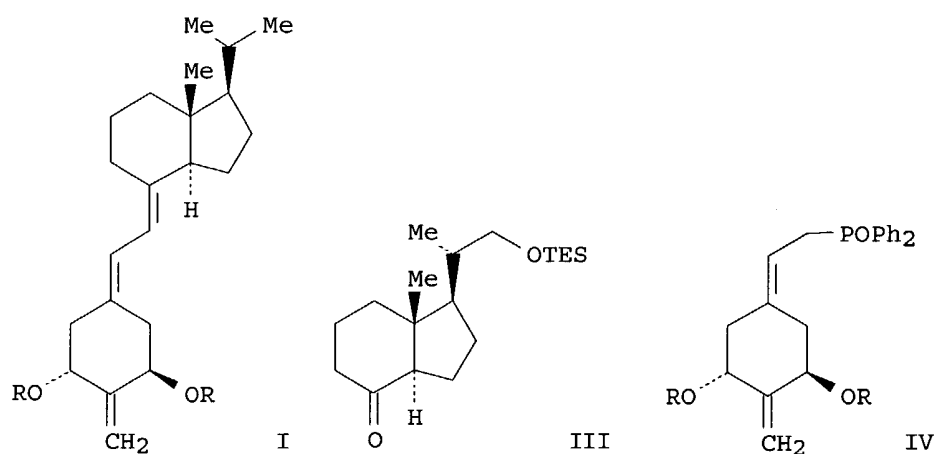
PRAI US 2002-369159P P 20020329 <--

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 2003191095	ICM	A61K031-59
	ICS	C07C401-00
	NCL	514167000; 552653000

OS CASREACT 139:307926; MARPAT 139:307926

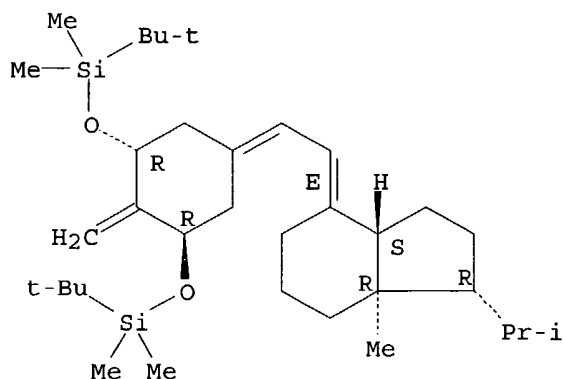
GI



- AB The present invention discloses a process for preparing 1α-hydroxy-2-methylene-19-nor-homopregnacalciferol [I; R = H (II)]. The method includes the steps of ozonating vitamin D2 to bicyclic ketone III, condensing III with an allylic phosphine oxide IV (R = TBDMS) to produce a protected 19-nor-pregnacalciferol analog, thereafter cleaving the protecting group to form 22-alc., converting the alc. to an ester, reducing the ester to 17α-isopropyl-19-nor-vitamin D analog I [R = TBDMS (V)], and finally deprotecting V to form II.
- ST homopregnacalciferol hydroxy methylene nor prepn vitamin D2;
 norhomopregnacalciferol prepn norpregnacalciferol analog
- IT Hydrolysis
 (acid; preparation of 1α-hydroxy-2-methylene-19-nor-homopregnacalciferol from vitamin D2)
- IT Hydrolysis
 (base; preparation of 1α-hydroxy-2-methylene-19-nor-homopregnacalciferol from vitamin D2)
- IT Sulfonylation
 (mesylation; preparation of 1α-hydroxy-2-methylene-19-nor-homopregnacalciferol from vitamin D2)
- IT Ozonization
 (preparation of 1α-hydroxy-2-methylene-19-nor-homopregnacalciferol from vitamin D2)
- IT Condensation reaction
 (stereoselective; between bicyclic ketone and an allylic phosphine oxide in preparation of 1α-hydroxy-2-methylene-19-nor-homopregnacalciferol)
- IT Oxidation
 Reduction

- (stereoselective; in preparation of 1 α -hydroxy-2-methylene-19-nor-homopregnacalciferol)
- IT Sulfonylation
(tosylation; in preparation of 1 α -hydroxy-2-methylene-19-nor-homopregnacalciferol from vitamin D2)
- IT 591-51-5, Phenyllithium
RL: RGT (Reagent); RACT (Reactant or reagent)
(for condensation between bicyclic ketone and an allylic phosphine oxide in preparation of 1 α -hydroxy-2-methylene-19-nor-homopregnacalciferol)
- IT 64190-52-9P 610304-66-0P 610304-67-1P 610304-68-2P 610304-69-3P
610304-70-6P **610304-71-7P**
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 1 α -hydroxy-2-methylene-19-nor-homopregnacalciferol from vitamin D2)
- IT **524067-22-9P**
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of 1 α -hydroxy-2-methylene-19-nor-homopregnacalciferol from vitamin D2)
- IT 50-14-6, Vitamin D2 98-59-9, p-Toluene sulfonyl chloride 79271-56-0, Triethylsilyl trifluoromethanesulfonate 213250-64-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of 1 α -hydroxy-2-methylene-19-nor-homopregnacalciferol from vitamin D2)
- IT 429-41-4, Tetrabutylammonium fluoride 16853-85-3, Lithium aluminum hydride 20039-37-6 24057-28-1, Pyridinium p-toluenesulfonate
RL: RGT (Reagent); RACT (Reactant or reagent)
(preparation of 1 α -hydroxy-2-methylene-19-nor-homopregnacalciferol from vitamin D2)
- IT **610304-71-7P**
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 1 α -hydroxy-2-methylene-19-nor-homopregnacalciferol from vitamin D2)
- RN 610304-71-7 HCAPLUS
- CN Silane, [[(1R,3R)-2-methylene-5-[(2E)-[(1R,3aS,7aR)-octahydro-7a-methyl-1-(1-methylethyl)-4H-inden-4-ylidene]ethylidene]-1,3-cyclohexanediyl]bis(oxy)]bis[(1,1-dimethylethyl)dimethyl- (9CI) (CA INDEX NAME)]

Absolute stereochemistry.
Double bond geometry as shown.



- IT **524067-22-9P**
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP

(Preparation)

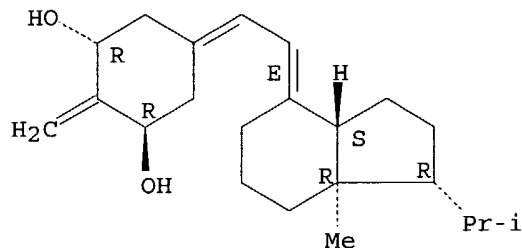
(preparation of 1 α -hydroxy-2-methylene-19-nor-homopregnacalciferol from vitamin D2)

RN 524067-22-9 HCAPLUS

CN 1,3-Cyclohexanediol, 2-methylene-5-[(2E)-[(1R,3aS,7aR)-octahydro-7a-methyl-1-(1-methylethyl)-4H-inden-4-ylidene]ethylidene]-, (1R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



L8 ANSWER 5 OF 9 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2003:491175 HCAPLUS

DN 139:53211

ED Entered STN: 27 Jun 2003

TI (20S)-1 α -hydroxy-2-methylene-19-nor-bishomopregnacalciferol and its therapeutic applications in the treatment of cancer, skin diseases and immune disorders

IN Deluca, Hector F.; Plum, Lori A.; Clagett-Dame, Margaret; Thoden, James B.; Holden, Hazel M.; Gowlugari, Sumithra; Grzywacz, Pawel

PA Wisconsin Alumni Research Foundation, USA

SO PCT Int. Appl., 59 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM C07C401-00

ICS A61K031-59; A61P011-06; A61P017-06; A61P035-00; A61P029-00; A61P037-00

CC 32-7 (Steroids)

Section cross-reference(s): 1, 2, 63, 75

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003051828	A2	20030626	WO 2002-US39715	20021212 <--
	WO 2003051828	A3	20030912		
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
	US 2003158157	A1	20030821	US 2002-78204	20020218 <--
	US 6627622	B2	20030930		
	US 2003204103	A1	20031030	US 2002-317467	20021212 <--
	US 2004033998	A1	20040219	US 2003-462272	20030616 <--
PRAI	US 2001-341138P	P	20011213		<--

US 2002-78204

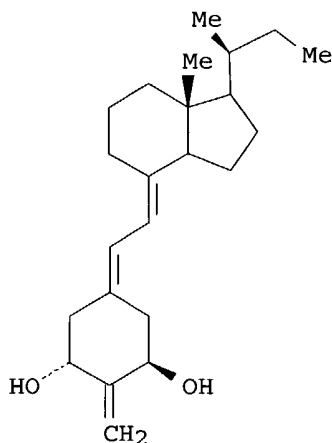
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20020218 <--

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2003051828	ICM	C07C401-00
	ICS	A61K031-59; A61P011-06; A61P017-06; A61P035-00; A61P029-00; A61P037-00

GI



I

AB This invention discloses (20S)-1 α -hydroxy-2-methylene-19-norbishomopregnacalciferol (I), pharmaceutical uses therefor, and a method of purifying this compound to obtain it in crystalline form. I exhibits pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as an anti-cancer agent and for the treatment of skin diseases such as psoriasis as well as skin conditions such as wrinkles, slack skin, dry skin and insufficient sebum secretion. I also has little, if any, calcemic activity and therefore may be used to treat immune disorders in humans as well as renal osteodystrophy.

ST homopregnacalciferol cancer immune disease skin calcemia treatment;
crystal structure homopregnacalciferol purifn renal osteodystrophy treatment

IT Anti-inflammatory agents

Antiasthmatics

Antidiabetic agents

Antirheumatic agents

Antitumor agents

Human

Monocyte

Psoriasis

((20S)-1 α -hydroxy-2-methylene-19-nor-bishomopregnacalciferol and its therapeutic applications in the treatment of cancer, skin diseases and immune disorders)

IT Vitamin D receptors

RL: BSU (Biological study, unclassified); BIOL (Biological study)

((20S)-1 α -hydroxy-2-methylene-19-nor-bishomopregnacalciferol and its therapeutic applications in the treatment of cancer, skin diseases and immune disorders)

IT Skin, disease

(aging, wrinkles; (20S)-1 α -hydroxy-2-methylene-19-nor-bishomopregnacalciferol and its therapeutic applications in the treatment of cancer, skin diseases and immune disorders)

IT Intestine, neoplasm

- (colon, treatment; (20S)-1 α -hydroxy-2-methylene-19-nor-bishomopregnacalciferol and its therapeutic applications in the treatment of cancer, skin diseases and immune disorders)
- IT Skin
(firmness; (20S)-1 α -hydroxy-2-methylene-19-nor-bishomopregnacalciferol and its therapeutic applications in the treatment of cancer, skin diseases and immune disorders)
- IT Transplant and Transplantation
(host-vs.-graft reaction, treatment; (20S)-1 α -hydroxy-2-methylene-19-nor-bishomopregnacalciferol and its therapeutic applications in the treatment of cancer, skin diseases and immune disorders)
- IT Intestine, disease
(inflammatory, treatment; (20S)-1 α -hydroxy-2-methylene-19-nor-bishomopregnacalciferol and its therapeutic applications in the treatment of cancer, skin diseases and immune disorders)
- IT Sebum
(insufficient secretion; (20S)-1 α -hydroxy-2-methylene-19-nor-bishomopregnacalciferol and its therapeutic applications in the treatment of cancer, skin diseases and immune disorders)
- IT Crystal structure
Crystallization
(of (20S)-1 α -hydroxy-2-methylene-19-nor-bishomopregnacalciferol and its therapeutic applications in the treatment of cancer, skin diseases and immune disorders)
- IT Drug delivery systems
(oral; (20S)-1 α -hydroxy-2-methylene-19-nor-bishomopregnacalciferol and its therapeutic applications in the treatment of cancer, skin diseases and immune disorders)
- IT Drug delivery systems
(parenterals; (20S)-1 α -hydroxy-2-methylene-19-nor-bishomopregnacalciferol and its therapeutic applications in the treatment of cancer, skin diseases and immune disorders)
- IT Bone, disease
(renal osteodystrophy, treatment; (20S)-1 α -hydroxy-2-methylene-19-nor-bishomopregnacalciferol and its therapeutic applications in the treatment of cancer, skin diseases and immune disorders)
- IT Drug delivery systems
(topical; (20S)-1 α -hydroxy-2-methylene-19-nor-bishomopregnacalciferol and its therapeutic applications in the treatment of cancer, skin diseases and immune disorders)
- IT Drug delivery systems
(transdermal; (20S)-1 α -hydroxy-2-methylene-19-nor-bishomopregnacalciferol and its therapeutic applications in the treatment of cancer, skin diseases and immune disorders)
- IT Asthma
Autoimmune disease
Diabetes mellitus
Leukemia
Mammary gland, neoplasm
Multiple sclerosis
Prostate gland, neoplasm
Rheumatoid arthritis
Transplant rejection
(treatment; (20S)-1 α -hydroxy-2-methylene-19-nor-bishomopregnacalciferol and its therapeutic applications in the treatment of cancer, skin diseases and immune disorders)
- IT 524067-21-8, (20S)-1 α -Hydroxy-2-methylene-19-norbishomopregnacalciferol
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
((20S)-1 α -hydroxy-2-methylene-19-nor-bishomopregnacalciferol and its therapeutic applications in the treatment of cancer, skin diseases and immune disorders)

IT 60-29-7, Diethylether, uses 67-63-0, Isopropanol, uses 67-64-1, Acetone, uses 67-66-3, Chloroform, uses 75-09-2, Dichloromethane, uses 141-78-6, Ethyl acetate, uses
 RL: NUU (Other use, unclassified); USES (Uses)
 (for purifying (20S)-1 α -hydroxy-2-methylene-19-nor-bishomopregnacalciferol)

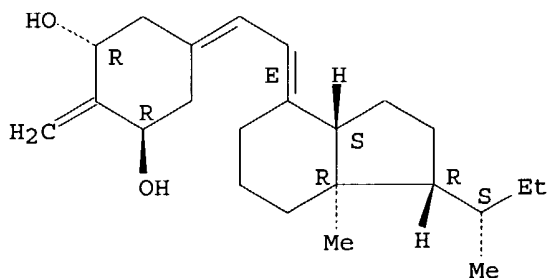
IT 7440-70-2, Calcium, biological studies
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (transport; effects of (20S)-1 α -hydroxy-2-methylene-19-nor-bishomopregnacalciferol on calcium levels in relation to their potential therapeutic uses)

IT 524067-21-8, (20S)-1 α -Hydroxy-2-methylene-19-norbishomopregnacalciferol
 RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 ((20S)-1 α -hydroxy-2-methylene-19-nor-bishomopregnacalciferol and its therapeutic applications in the treatment of cancer, skin diseases and immune disorders)

RN 524067-21-8 HCAPLUS

CN 1,3-Cyclohexanediol, 2-methylene-5-[(2E)-[(1R,3aS,7aR)-octahydro-7a-methyl-1-[(1S)-1-methylpropyl]-4H-inden-4-ylidene]ethylidene]-, (1R,3R)- (9CI)
 (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.



L8 ANSWER 6 OF 9 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2003:390842 HCAPLUS

DN 138:363223

ED Entered STN: 22 May 2003

TI Methods for the uses of 1 α -Hydroxy-2-methylene-19-nor-pregnacalciferol in the treatment of cancer, skin diseases and immune disorders

IN Deluca, Hector F.; Plum, Lori A.; Clagett-Dame, Margaret

PA Wisconsin Alumni Research Foundation, USA

SO U.S., 13 pp.
 CODEN: USXXAM

DT Patent

LA English

IC ICM A61K031-59
 ICS C07C401-00

NCL 514167000; 552653000

CC 2-10 (Mammalian Hormones)
 Section cross-reference(s): 14

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6566352	B1	20030520	US 2002-77916	20020218 <--
	WO 2003075932	A1	20030918	WO 2002-US39390	20021210 <--
	WO 2003075932	C1	20040401		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
 CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
 GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
 LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
 PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA,
 UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
 CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
 PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
 MR, NE, SN, TD, TG

PRAI US 2002-77916 A 20020218 <--

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 6566352	ICM	A61K031-59
	ICS	C07C401-00
	NCL	514167000; 552653000

AB This invention discloses 1 α -hydroxy-2-methylene-19-nor-pregnacalciferol and pharmaceutical uses therefor. This compound exhibits pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as an anti-cancer agent and for the treatment of skin diseases such as psoriasis as well as skin conditions such as wrinkles, slack skin, dry skin and insufficient sebum secretion. This compound also has little, if any, calcemic activity and therefore may be used to treat immune disorders in humans as well as renal osteodystrophy.

ST vitamin D deriv treatment cancer immune diseases skin calcemia

IT Skin, disease
 (aging, wrinkles; methods for using 1 α -Hydroxy-2-methylene-19-nor-pregnacalciferol in treatment of cancer, skin diseases and immune disorders)

IT Vitamin D receptors
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (binding of vitamin D compds.; effects of vitamin D compds. on cell differentiation and calcium levels in relation to their potential pharmaceutical uses)

IT Bone
 (calcium mobilization; effects of vitamin D compds. on cell differentiation and calcium levels in relation to their potential pharmaceutical uses)

IT Intestine
 (calcium transport; effects of vitamin D compds. on cell differentiation and calcium levels in relation to their potential pharmaceutical uses)

IT Intestine, neoplasm
 (colon; methods for using 1 α -Hydroxy-2-methylene-19-nor-pregnacalciferol in treatment of cancer, skin diseases and immune disorders)

IT Skin, disease
 (dry; methods for using 1 α -Hydroxy-2-methylene-19-nor-pregnacalciferol in treatment of cancer, skin diseases and immune disorders)

IT Cell differentiation
 (effects of vitamin D compds. on cell differentiation and calcium levels in relation to their potential pharmaceutical uses)

IT Transplant and Transplantation
 (graft-vs.-host reaction; methods for using 1 α -Hydroxy-2-methylene-19-nor-pregnacalciferol in treatment of cancer, skin diseases and immune disorders)

IT Intestine, disease
 (inflammatory; methods for using 1 α -Hydroxy-2-methylene-19-nor-pregnacalciferol in treatment of cancer, skin diseases and immune disorders)

IT Sebum
(insufficient secretion; methods for using 1 α -Hydroxy-2-methylene-19-nor-pregnacalciferol in treatment of cancer, skin diseases and immune disorders)

IT Anti-inflammatory agents
Antiasthmatics
Antidiabetic agents
Antirheumatic agents
Antitumor agents
Asthma
Autoimmune disease
Diabetes mellitus
Human
Inflammation
Leukemia
Lupus erythematosus
Mammary gland, neoplasm
Multiple sclerosis
Prostate gland, neoplasm
Psoriasis
Rheumatoid arthritis
Skin, disease
Skin preparations (pharmaceutical)
Transplant rejection
(methods for using 1 α -Hydroxy-2-methylene-19-nor-pregnacalciferol in treatment of cancer, skin diseases and immune disorders)

IT Bone, disease
(renal osteodystrophy; methods for using 1 α -Hydroxy-2-methylene-19-nor-pregnacalciferol in treatment of cancer, skin diseases and immune disorders)

IT Skin, disease
(slackness; methods for using 1 α -Hydroxy-2-methylene-19-nor-pregnacalciferol in treatment of cancer, skin diseases and immune disorders)

IT 1406-16-2D, Vitamin D, derivs. 32222-06-3, 1 α ,25-Dihydroxyvitamin D3 130447-37-9 524067-21-8 524067-22-9
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(effects of vitamin D compds. on cell differentiation and calcium levels in relation to their potential pharmaceutical uses)

IT 524067-20-7
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods for using 1 α -Hydroxy-2-methylene-19-nor-pregnacalciferol in treatment of cancer, skin diseases and immune disorders)

IT 7440-70-2, Calcium, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(transport; effects of vitamin D compds. on cell differentiation and calcium levels in relation to their potential pharmaceutical uses)

RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Anon; WO 9601811 1996 HCAPLUS
(2) Brown; Kidney International 1990, V38(Suppl 29), PS-22
(3) Deluca; US 4800198 A 1989 HCAPLUS
(4) Deluca; US 5089641 A 1992 HCAPLUS
(5) Deluca; US 5536713 A 1996 HCAPLUS
(6) Deluca; US 5578587 A 1996 HCAPLUS
(7) Deluca; US 5587497 A 1996 HCAPLUS
(8) Deluca; US 5843928 A 1998 HCAPLUS
(9) Deluca; US 5936133 A 1999 HCAPLUS
(10) Deluca; US 5945410 A 1999 HCAPLUS
(11) Hareau; Tetrahedron Letters 2000, V41, P2385 HCAPLUS
(12) Hennessy; US 5840718 A 1998 HCAPLUS
(13) Kutner; US 5817648 A 1998 HCAPLUS

- (14) Miyamoto; US 4666634 A 1987 HCAPLUS
 (15) Posner; J Org Chem 1995, V60(4617), P4617
 (16) Sicinski; J Med Chem 1998, V41, P4662 HCAPLUS

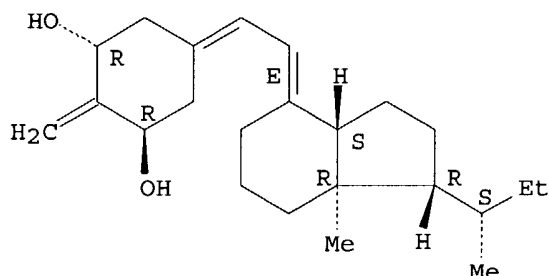
IT 524067-21-8 524067-22-9

RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (effects of vitamin D compds. on cell differentiation and calcium
 levels in relation to their potential pharmaceutical uses)

RN 524067-21-8 HCAPLUS

CN 1,3-Cyclohexanediol, 2-methylene-5-[(2E)-[(1R,3aS,7aR)-octahydro-7a-methyl-1-[(1S)-1-methylpropyl]-4H-inden-4-ylidene]ethylidene]-, (1R,3R)- (9CI)
 (CA INDEX NAME)

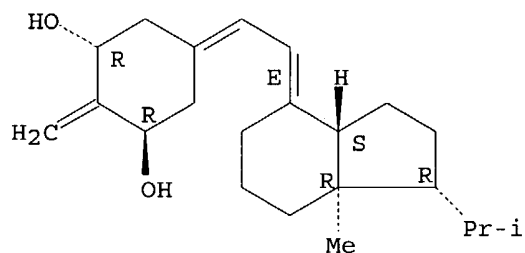
Absolute stereochemistry.
 Double bond geometry as shown.



RN 524067-22-9 HCAPLUS

CN 1,3-Cyclohexanediol, 2-methylene-5-[(2E)-[(1R,3aS,7aR)-octahydro-7a-methyl-1-(1-methylethyl)-4H-inden-4-ylidene]ethylidene]-, (1R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.



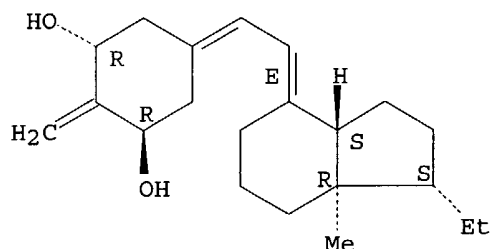
IT 524067-20-7

RL: BSU (Biological study, unclassified); PAC (Pharmacological activity);
 THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (methods for using 1 α -Hydroxy-2-methylene-19-nor-pregnacalciferol
 in treatment of cancer, skin diseases and immune disorders)

RN 524067-20-7 HCAPLUS

CN 1,3-Cyclohexanediol, 5-[(2E)-[(1S,3aS,7aR)-1-ethyloctahydro-7a-methyl-4H-inden-4-ylidene]ethylidene]-2-methylene-, (1R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.



L8 ANSWER 7 OF 9 HCAPLUS COPYRIGHT 2004 ACS on STN
 AN 2003:249861 HCAPLUS
 DN 139:317525
 ED Entered STN: 01 Apr 2003
 TI Interaction between vitamin D receptor and vitamin D ligands
 two-dimensional alanine scanning mutational analysis
 AU Choi, Mihwa; Yamamoto, Keiko; Itoh, Toshimasa; Makishima, Makoto;
 Mangelsdorf, David J.; Moras, Dino; DeLuca, Hector F.; Yamada,
 Sachiko
 CS Institute of Biomaterials and Bioengineering, Tokyo Medical and Dental
 University, Chiyoda-ku, Tokyo, 101-0062, Japan
 SO Chemistry & Biology (2003), 10(3), 261-270
 CODEN: CBOLE2; ISSN: 1074-5521
 PB Cell Press
 DT Journal
 LA English
 CC 2-1 (Mammalian Hormones)
 AB We present a new method to investigate the details of interaction between
 vitamin D nuclear receptor (VDR) and various ligands, namely a
 two-dimensional alanine scanning mutational anal. In this method, the
 transactivation of various ligands is studied in conjunction with a series
 of alanine scanning mutations of the residues lining the ligand binding
 pocket (LBP) of VDR, and the complete set of results is profiled in a
 patch table. We investigated examples from four structurally diverse
 groups of known VDR ligands: the native vitamin D hormone and two compds.
 with the same side chain configuration; four 20-epi compds.; three 19-nor
 compds.; and two nonsecosteroids. The patch table of the results
 indicates characteristics of each group in terms of its interaction with
 18 LBP residues. We demonstrate the validity of this approach by
 application to docking studies of the two nonsecosteroids.
 ST vitamin D receptor structure activity ligand binding alanine mutagenesis
 IT Simulation and Modeling, physicochemical
 (docking models of VDR ligands; two-dimensional alanine scanning
 mutational anal. and modeling of the interaction between vitamin D
 receptor (VDR) its ligands)
 IT Structure-activity relationship
 (ligand-binding; two-dimensional alanine scanning mutational anal. and
 modeling of the interaction between vitamin D receptor (VDR) its
 ligands)
 IT Protein motifs
 (of VDR; two-dimensional alanine scanning mutational anal. and modeling
 of the interaction between vitamin D receptor (VDR) its ligands)
 IT Mutagenesis
 (site-directed; two-dimensional alanine scanning mutational anal. and
 modeling of the interaction between vitamin D receptor (VDR) its
 ligands)
 IT Configuration
 Secondary structure
 (two-dimensional alanine scanning mutational anal. and modeling of the
 interaction between vitamin D receptor (VDR) its ligands)

IT Vitamin D receptors
 RL: PRP (Properties)
 (two-dimensional alanine scanning mutational anal. and modeling of the interaction between vitamin D receptor (VDR) its ligands)

IT 56-41-7, L-Alanine, properties
 RL: PRP (Properties)
 (mutational anal.; two-dimensional alanine scanning mutational anal. and modeling of the interaction between vitamin D receptor (VDR) its ligands)

IT 434-13-9 1553-56-6 32222-06-3 103909-75-7 104121-92-8
 131875-08-6, KH 1060 134523-84-5 177766-94-8 195051-26-4
 213250-70-5 213312-43-7 **524067-22-9**
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (two-dimensional alanine scanning mutational anal. and modeling of the interaction between vitamin D receptor (VDR) its ligands)

RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

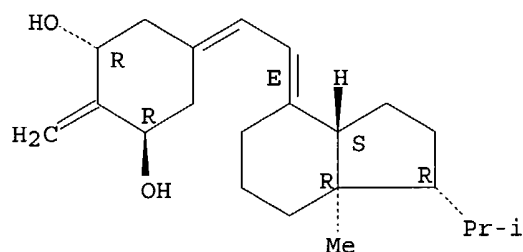
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IT **524067-22-9**
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (two-dimensional alanine scanning mutational anal. and modeling of the interaction between vitamin D receptor (VDR) its ligands)

RN 524067-22-9 HCAPLUS

CN 1,3-Cyclohexanediol, 2-methylene-5-[(2E)-[(1R,3aS,7aR)-octahydro-7a-methyl-1-(1-methylethyl)-4H-inden-4-ylidene]ethylidene]-, (1R,3R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.



L8 ANSWER 8 OF 9 HCAPLUS COPYRIGHT 2004 ACS on STN
 AN 2002:332679 HCAPLUS
 DN 136:335278
 ED Entered STN: 03 May 2002
 TI 1 α -Hydroxy-2-methylene-19-nor-homopregnacalciferol and its
 therapeutic uses
 IN DeLuca, Hector F.; Sicinski, Rafal R.; Gowlugari,
 Sumithra; Plum, Lori A.; Clagett-Dame, Margaret
 PA USA
 SO U.S. Pat. Appl. Publ., 14 pp., Cont.-in-part of U. S. Ser. No. 657,828.
 CODEN: USXXCO
 DT Patent
 LA English
 IC ICM A61K031-59
 NCL 514167000
 CC 1-12 (Pharmacology)
 FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002052350	A1	20020502	US 2001-878438	20010611 <--
	US 6440953	B2	20020827		
	US 2002183289	A1	20021205	US 2002-165123	20020607 <--
	US 6579861	B2	20030617		
PRAI	US 2000-657828	A2	20000908	<--	
	US 2001-878438	A3	20010611	<--	

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 2002052350	ICM	A61K031-59
	NCL	514167000
US 2002052350	ECLA	A61K007/48C4D <--
US 2002183289	ECLA	A61K007/48C4D <--

AB The invention discloses 1 α -hydroxy-2-methylene-19-nor-homopregnacalciferol and its pharmaceutical uses. This compound exhibits pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as an anti-cancer agent and for the treatment of skin diseases such as psoriasis as well as skin conditions such as wrinkles, slack skin, dry skin and insufficient sebum secretion. This compound also has little, if any, calcemic activity and therefore may be used to treat immune disorders in humans as well as renal osteodystrophy.

ST hydroxymethylenenorhomopregnacalciferol cell proliferation differentiation therapeutic; cancer skin disease immune disorder hydroxymethylenenorhomopregnacalciferol; renal osteodystrophy hydroxymethylenenorhomopregnacalciferol

IT Animal cell line
 (HL-60; hydroxymethylenenorhomopregnacalciferol and therapeutic use)

IT Animal cell line
 (LLC; hydroxymethylenenorhomopregnacalciferol and therapeutic use)

IT Animal cell line

(ROS; hydroxymethylenenorhomopregnacalciferol and therapeutic use)

IT Skin, disease
(aging, wrinkles; hydroxymethylenenorhomopregnacalciferol and therapeutic use)

IT Bone
(calcium mobilization; hydroxymethylenenorhomopregnacalciferol and therapeutic use)

IT Biological transport
(calcium; hydroxymethylenenorhomopregnacalciferol and therapeutic use)

IT Intestine, neoplasm
(colon, inhibitors; hydroxymethylenenorhomopregnacalciferol and therapeutic use)

IT Antitumor agents
(colon; hydroxymethylenenorhomopregnacalciferol and therapeutic use)

IT Drugs
(gastrointestinal; hydroxymethylenenorhomopregnacalciferol and therapeutic use)

IT Transplant and Transplantation
(host-vs.-graft reaction; hydroxymethylenenorhomopregnacalciferol and therapeutic use)

IT Anti-inflammatory agents
Antiasthmatics
Antidiabetic agents
Antirheumatic agents
Autoimmune disease
Human
Lupus erythematosus
Psoriasis
Skin
Transcription, genetic
Transplant rejection
(hydroxymethylenenorhomopregnacalciferol and therapeutic use)

IT Vitamin D receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(hydroxymethylenenorhomopregnacalciferol and therapeutic use)

IT Cell differentiation
(inducers; hydroxymethylenenorhomopregnacalciferol and therapeutic use)

IT Intestine, disease
(inflammatory; hydroxymethylenenorhomopregnacalciferol and therapeutic use)

IT Antitumor agents
(leukemia; hydroxymethylenenorhomopregnacalciferol and therapeutic use)

IT Antitumor agents
(mammary gland; hydroxymethylenenorhomopregnacalciferol and therapeutic use)

IT Mammary gland
Prostate gland
(neoplasm, inhibitors; hydroxymethylenenorhomopregnacalciferol and therapeutic use)

IT Drug delivery systems
(oral; hydroxymethylenenorhomopregnacalciferol and therapeutic use)

IT Drug delivery systems
(parenterals; hydroxymethylenenorhomopregnacalciferol and therapeutic use)

IT Antitumor agents
(prostate gland; hydroxymethylenenorhomopregnacalciferol and therapeutic use)

IT Bone, disease
(renal osteodystrophy; hydroxymethylenenorhomopregnacalciferol and therapeutic use)

IT Sebum
(secretion; hydroxymethylenenorhomopregnacalciferol and therapeutic use)

IT Multiple sclerosis
(therapeutic agents; hydroxymethylenenorhomopregnacalciferol and therapeutic use)

IT Drug delivery systems
(topical; hydroxymethylenenorhomopregnacalciferol and therapeutic use)

IT Drug delivery systems
(transdermal; hydroxymethylenenorhomopregnacalciferol and therapeutic use)

IT 32222-06-3, 1 α ,25-Dihydroxyvitamin D3 213250-70-5
RL: PAC (Pharmacological activity); BIOL (Biological study)
(hydroxymethylenenorhomopregnacalciferol and therapeutic use)

IT 403647-27-8
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hydroxymethylenenorhomopregnacalciferol and therapeutic use)

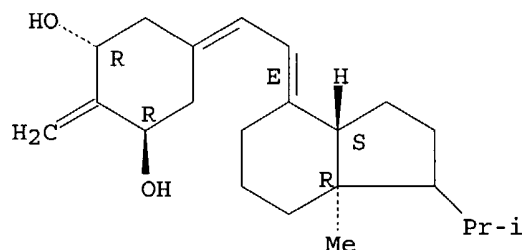
IT 7440-70-2, Calcium, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(intestinal transport; hydroxymethylenenorhomopregnacalciferol and therapeutic use)

IT 403647-27-8
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hydroxymethylenenorhomopregnacalciferol and therapeutic use)

RN 403647-27-8 HCAPLUS

CN 1,3-Cyclohexanediol, 2-methylene-5-[(2E)-[(3aS,7aR)-octahydro-7a-methyl-1-(1-methylethyl)-4H-inden-4-ylidene]ethylidene]-, (1R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L8 ANSWER 9 OF 9 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2002:184908 HCAPLUS

DN 136:226818

ED Entered STN: 15 Mar 2002

TI 1Alpha-Hydroxy-2-methylene-19-nor-homopregnacalciferol and its therapeutic applications

IN Deluca, Hector F.; Sicinski, Rafal R.; Gowlugari, Sumithra; Plum, Lori A.; Clagett-Dame, Margaret

PA Wisconsin Alumni Research Foundation, USA

SO PCT Int. Appl., 31 pp.
CODEN: PIXXD2

DT Patent

LA English

IC ICM A61K031-59
ICS C07C401-00

CC 1-12 (Pharmacology)
Section cross-reference(s): 2, 62, 63

FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI WO 2002020021 A1 20020314 WO 2001-US18710 20010611 <--
 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
 CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
 HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
 LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
 SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU,
 ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
 DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
 BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
 AU 2001075445 A5 20020322 AU 2001-75445 20010611 <--
 EP 1315504 A1 20030604 EP 2001-942154 20010611 <--
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
 BR 2001013703 A 20030722 BR 2001-13703 20010611 <--
 JP 2004512276 T2 20040422 JP 2002-524505 20010611 <--
 PRAI US 2000-657828 A 20000908 <--
 WO 2001-US18710 W 20010611 <--

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2002020021	ICM	A61K031-59
	ICS	C07C401-00
JP 2004512276	FTERM	4C086/AA01; 4C086/AA02; 4C086/AA03; 4C086/DA15; 4C086/MA01; 4C086/MA04; 4C086/NA14; 4C086/ZA02; 4C086/ZA59; 4C086/ZA66; 4C086/ZA89; 4C086/ZA96; 4C086/ZB08; 4C086/ZB15; 4C086/ZB26; 4C086/ZB27; 4C086/ZC23; 4C086/ZC35; 4H006/AA01; 4H006/AA03; 4H006/AB22; 4H006/AB27; 4H006/AB28; 4H006/UA13 <--
AB	This invention discloses 1 α -hydroxy-2-methylene-19-nor-homopregnacalciferol and pharmaceutical uses therefor. This compound exhibits pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte this evidencing use as an anti-cancer agent and for the treatment of skin diseases such as psoriasis as well as skin conditions such as wrinkles, slack skin, dry skin and insufficient sebum secretion. This compound also has little, if any calcemic activity and therefore may be used to treat immune disorders in humans as well as renal osteodystrophy.	
ST	homopregnacalciferol deriv therapeutic cancer immune disorder; renal osteodystrophy treatment homopregnacalciferol deriv; skin disease treatment homopregnacalciferol deriv	
IT	Anti-inflammatory agents Antiasthmatics Antidiabetic agents Antirheumatic agents Antitumor agents Human Monocyte (1 α -hydroxy-2-methylene-19-nor-homopregnacalciferol and therapeutic applications)	
IT	Vitamin D receptors RL: BSU (Biological study, unclassified); BIOL (Biological study) (1 α -hydroxy-2-methylene-19-nor-homopregnacalciferol and therapeutic applications)	
IT	Animal cell line (HL-60, cell differentiation; 1 α -hydroxy-2-methylene-19-nor-homopregnacalciferol and therapeutic applications)	
IT	Transcriptional regulation (activation; 1 α -hydroxy-2-methylene-19-nor-homopregnacalciferol and therapeutic applications)	
IT	Bone (calcium mobilization; 1 α -hydroxy-2-methylene-19-nor-homopregnacalciferol and therapeutic applications)	

IT Kidney
(cells; 1 α -hydroxy-2-methylene-19-nor-homopregnacalciferol and therapeutic applications)

IT Intestine, neoplasm
(colon, inhibitors; 1 α -hydroxy-2-methylene-19-nor-homopregnacalciferol and therapeutic applications)

IT Antitumor agents
(colon; 1 α -hydroxy-2-methylene-19-nor-homopregnacalciferol and therapeutic applications)

IT Skin
(conditions wrinkles and slack skin, treatment of; 1 α -hydroxy-2-methylene-19-nor-homopregnacalciferol and therapeutic applications)

IT Immunity
(disorder, treatment of; 1 α -hydroxy-2-methylene-19-nor-homopregnacalciferol and therapeutic applications)

IT Skin, disease
(dry, treatment of; 1 α -hydroxy-2-methylene-19-nor-homopregnacalciferol and therapeutic applications)

IT Transplant and Transplantation
(host-vs.-graft reaction, treatment of; 1 α -hydroxy-2-methylene-19-nor-homopregnacalciferol and therapeutic applications)

IT Cell differentiation
(inducers; 1 α -hydroxy-2-methylene-19-nor-homopregnacalciferol and therapeutic applications)

IT Intestine, disease
(inflammatory, treatment of; 1 α -hydroxy-2-methylene-19-nor-homopregnacalciferol and therapeutic applications)

IT Cell proliferation
(inhibition, of undifferentiated cells; 1 α -hydroxy-2-methylene-19-nor-homopregnacalciferol and therapeutic applications)

IT Sebum
(insufficient secretion of, treatment of; 1 α -hydroxy-2-methylene-19-nor-homopregnacalciferol and therapeutic applications)

IT Antitumor agents
(leukemia; 1 α -hydroxy-2-methylene-19-nor-homopregnacalciferol and therapeutic applications)

IT Antitumor agents
(mammary gland; 1 α -hydroxy-2-methylene-19-nor-homopregnacalciferol and therapeutic applications)

IT Mammary gland
Prostate gland
(neoplasm, inhibitors; 1 α -hydroxy-2-methylene-19-nor-homopregnacalciferol and therapeutic applications)

IT Antidiabetic agents
Drug delivery systems
(oral; 1 α -hydroxy-2-methylene-19-nor-homopregnacalciferol and therapeutic applications)

IT Drug delivery systems
(parenterals; 1 α -hydroxy-2-methylene-19-nor-homopregnacalciferol and therapeutic applications)

IT Antitumor agents
(prostate gland; 1 α -hydroxy-2-methylene-19-nor-homopregnacalciferol and therapeutic applications)

IT Bone, disease
(renal osteodystrophy, treatment of; 1 α -hydroxy-2-methylene-19-nor-homopregnacalciferol and therapeutic applications)

IT Drug delivery systems
(topical; 1 α -hydroxy-2-methylene-19-nor-homopregnacalciferol and therapeutic applications)

IT Drug delivery systems
(transdermal; 1 α -hydroxy-2-methylene-19-nor-homopregnacalciferol and therapeutic applications)

IT Autoimmune disease

Lupus erythematosus
 Multiple sclerosis
 Psoriasis
 Skin, disease
 Transplant rejection
 (treatment of; 1 α -hydroxy-2-methylene-19-nor-homopregnacalciferol
 and therapeutic applications)

IT 403647-27-8

RL: BSU (Biological study, unclassified); COS (Cosmetic use); DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (1 α -hydroxy-2-methylene-19-nor-homopregnacalciferol and therapeutic applications)

IT 7440-70-2, Calcium, biological studies

RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
 (calcemic; 1 α -hydroxy-2-methylene-19-nor-homopregnacalciferol and therapeutic applications)

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

- (1) Brown, A; KIDNEY INTERNATIONAL 1990, V38(29), PS-22
- (2) Hareau, G; TETRAHEDRON LETTERS 2000, V41(14), P2385 HCAPLUS
- (3) Rafal, S; US 5843928 A 1998 HCAPLUS
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- (5) Sicinski; JOURNAL OF MEDICINAL CHEMISTRY 1998, V41, P4662 HCAPLUS
- (6) Sicinski, R; US 5936133 A 1999 HCAPLUS

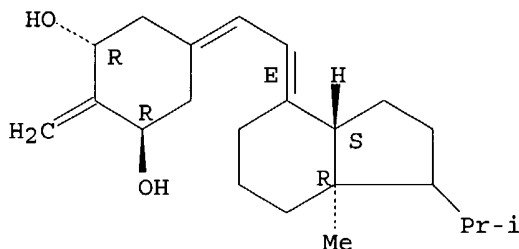
IT 403647-27-8

RL: BSU (Biological study, unclassified); COS (Cosmetic use); DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (1 α -hydroxy-2-methylene-19-nor-homopregnacalciferol and therapeutic applications)

RN 403647-27-8 HCAPLUS

CN 1,3-Cyclohexanediol, 2-methylene-5-[(2E)-[(3aS,7aR)-octahydro-7a-methyl-1-(1-methylethyl)-4H-inden-4-ylidene]ethylidene]-, (1R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.



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FILE 'USPATFULL' ENTERED AT 10:23:11 ON 25 AUG 2004

CA INDEXING COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'USPAT2' ENTERED AT 10:23:11 ON 25 AUG 2004

CA INDEXING COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

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L10 ANSWER 1 OF 18 USPATFULL on STN

AN 2004:197374 USPATFULL
 TI (20S)-1alpha-hydroxy-2alpha-methyl and 2beta-methyl-19-nor-vitamin D3 and their uses
 IN DeLuca, Hector F., Deerfield, WI, UNITED STATES
 Sicinski, Rafal R., Warsaw, POLAND
 Grzywacz, Pawel K., Madison, WI, UNITED STATES
 PA Wisconsin Alumni Research Foundation, Madison, WI (U.S. corporation)
 PI US 2004152680 A1 20040805
 AI US 2004-763029 A1 20040122 (10)
 RLI Division of Ser. No. US 2002-127180, filed on 22 Apr 2002, PENDING
 DT Utility
 FS APPLICATION
 LREP ANDRUS, SCEALES, STARKE & SAWALL, LLP, 100 EAST WISCONSIN AVENUE, SUITE 1100, MILWAUKEE, WI, 53202
 CLMN Number of Claims: 77
 ECL Exemplary Claim: 1
 DRWN 1 Drawing Page(s)
 LN.CNT 981

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention discloses (20S)-1 α -hydroxy-2 α -methyl-19-nor-vitamin D.sub.3 and (20S)-1 α -hydroxy-2 α -methyl-19-nor-vitamin D.sub.3 and pharmaceutical uses therefor. These compounds exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as an anti-cancer agent and for the treatment of skin diseases such as psoriasis as well as skin conditions such as wrinkles, slack skin, dry skin and insufficient sebum secretion. These compounds also have very significant calcemic activity and therefore may be used to treat immune disorders in humans as well as metabolic bone diseases such as osteoporosis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 618104-22-6P

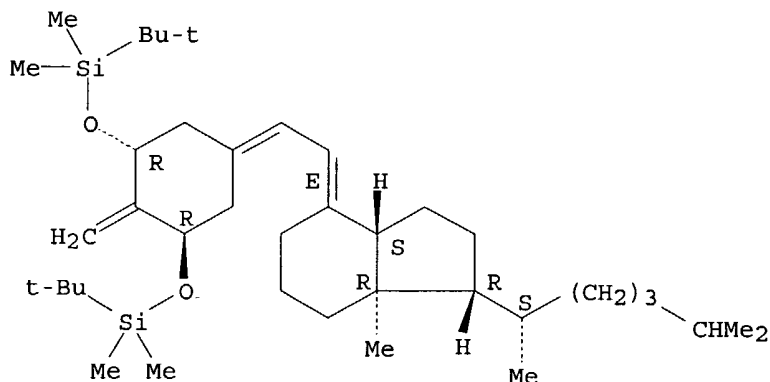
(nor-vitamin D3 derivs. and pharmaceutical uses)

RN 618104-22-6 USPATFULL

CN Silane, [[(1 α ,3 β ,7E,20S)-2-methylene-19-nor-9,10-secocholesta-5,7,10(19)-triene-1,3-diyl]bis(oxy)]bis(1,1-dimethylethyl)dimethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



L10 ANSWER 2 OF 18 USPATFULL on STN

AN 2004:197373 USPATFULL

TI (20S)-1alpha-hydroxy-2alpha-methyl and 2beta-methyl-19-nor-vitamin D3 and their uses

IN DeLuca, Hector F., Deerfield, WI, UNITED STATES
 Sicinski, Rafal R., Warsaw, POLAND
 Grzywacz, Pawel K., Madison, WI, UNITED STATES
 PA Wisconsin Alumni Research Foundation, Madison, WI (U.S. corporation)
 PI US 2004152679 A1 20040805
 AI US 2004-763023 A1 20040122 (10)
 RLI Division of Ser. No. US 2002-127180, filed on 22 Apr 2002, PENDING
 DT Utility
 FS APPLICATION
 LREP ANDRUS, SCEALES, STARKE & SAWALL, LLP, 100 EAST WISCONSIN AVENUE, SUITE
 1100, MILWAUKEE, WI, 53202
 CLMN Number of Claims: 77
 ECL Exemplary Claim: 1
 DRWN 1 Drawing Page(s)
 LN.CNT 979

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention discloses (20S)-1 α -hydroxy-2 α -methyl-19-nor-vitamin D.sub.3 and (20S)-1 α -hydroxy-2 β -methyl-19-nor-vitamin D.sub.3 and pharmaceutical uses therefor. These compounds exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as an anti-cancer agent and for the treatment of skin diseases such as psoriasis as well as skin conditions such as wrinkles, slack skin, dry skin and insufficient sebum secretion. These compounds also have very significant calcemic activity and therefore may be used to treat immune disorders in humans as well as metabolic bone diseases such as osteoporosis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 618104-22-6P

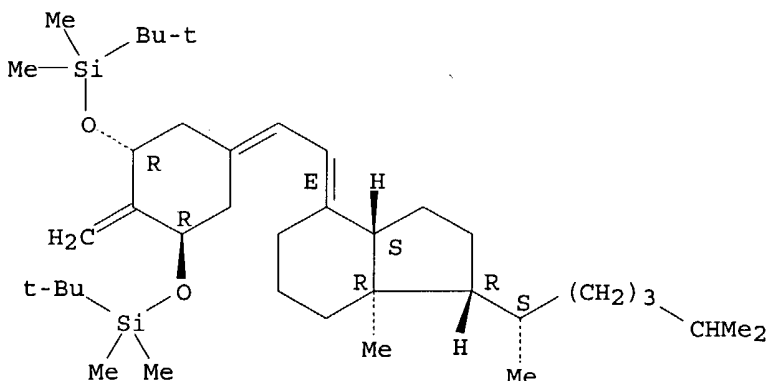
(nor-vitamin D3 derivs. and pharmaceutical uses)

RN 618104-22-6 USPATFULL

CN Silane, [[(1 α ,3 β ,7E,20S)-2-methylene-19-nor-9,10-secocholesta-5,7,10(19)-triene-1,3-diyl]bis(oxy)]bis(1,1-dimethylethyl)dimethyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



L10 ANSWER 3 OF 18 USPATFULL on STN

AN 2004:197372 USPATFULL

TI (20S)-1 α -hydroxy-2 α -methyl and 2 β -methyl-19-nor-vitamin D3 and their uses

IN DeLuca, Hector F., Deerfield, WI, UNITED STATES
 Sicinski, Rafal R., Warsaw, POLAND
 Grzywacz, Pawel K., Madison, WI, UNITED STATES

PA Wisconsin Alumni Research Foundation, Madison, WI (U.S. corporation)
 PI US 2004152678 A1 20040805
 AI US 2004-762911 A1 20040122 (10)
 RLI Division of Ser. No. US 2002-127180, filed on 22 Apr 2002, PENDING
 DT Utility
 FS APPLICATION
 LREP ANDRUS, SCEALES, STARKE & SAWALL, LLP, 100 EAST WISCONSIN AVENUE, SUITE
 1100, MILWAUKEE, WI, 53202
 CLMN Number of Claims: 77
 ECL Exemplary Claim: 1
 DRWN 1 Drawing Page(s)
 LN.CNT 977

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention discloses (20S)-1 α -hydroxy-2 α -methyl-19-nor-vitamin D.sub.3 and (20S)-1 α -hydroxy-2 β -methyl-19-nor-vitamin D.sub.3 and pharmaceutical uses therefor. These compounds exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as an anti-cancer agent and for the treatment of skin diseases such as psoriasis as well as skin conditions such as wrinkles, slack skin, dry skin and insufficient sebum secretion. These compounds also have very significant calcemic activity and therefore may be used to treat immune disorders in humans as well as metabolic bone diseases such as osteoporosis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 618104-22-6P

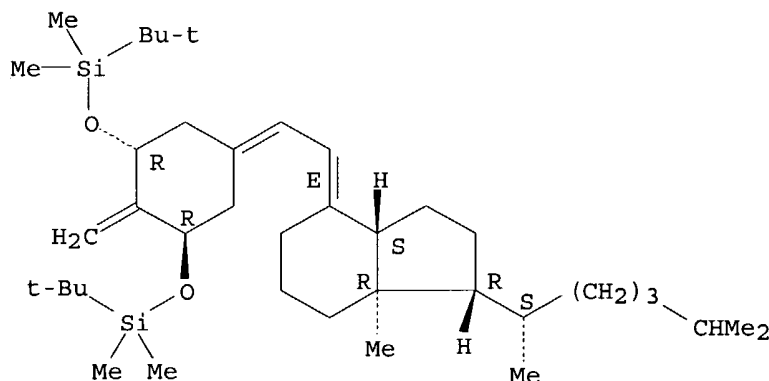
(nor-vitamin D3 derivs. and pharmaceutical uses)

RN 618104-22-6 USPATFULL

CN Silane, [[[1 α ,3 β ,7E,20S)-2-methylene-19-nor-9,10-secocholesta-5,7,10(19)-triene-1,3-diyl]bis(oxy)]bis(1,1-dimethylethyl)dimethyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



L10 ANSWER 4 OF 18 USPATFULL on STN

AN 2004:197371 USPATFULL

TI (20S)-1 α -hydroxy-2 α -methl and 2 β -methyl-19-nor-vitamin D3 and their uses

IN DeLuca, Hector F., Deerfield, WI, UNITED STATES

Sicinski, Rafal R., Warsaw, POLAND

Grzywacz, Pawel K., Madison, WI, UNITED STATES

PA Wisconsin Alumni Research Foundation, Madison, WI (U.S. corporation)

PI US 2004152677 A1 20040805

AI US 2004-762906 A1 20040122 (10)

RLI Division of Ser. No. US 2002-127180, filed on 22 Apr 2002, PENDING
 DT Utility
 FS APPLICATION
 LREP ANDRUS, SCEALES, STARKE & SAWALL, LLP, 100 EAST WISCONSIN AVENUE, SUITE
 1100, MILWAUKEE, WI, 53202
 CLMN Number of Claims: 77
 ECL Exemplary Claim: 1
 DRWN 1 Drawing Page(s)
 LN.CNT 980

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention discloses (20S)-1 α -hydroxy-2 α -methyl-19-nor-vitamin D.sub.3 and (20S)-1 α -hydroxy-2 β -methyl-19-nor-vitamin D.sub.3 and pharmaceutical uses therefor. These compounds exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as an anti-cancer agent and for the treatment of skin diseases such as psoriasis as well as skin conditions such as wrinkles, slack skin, dry skin and insufficient sebum secretion. These compounds also have very significant calcemic activity and therefore may be used to treat immune disorders in humans as well as metabolic bone diseases such as osteoporosis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 618104-22-6P

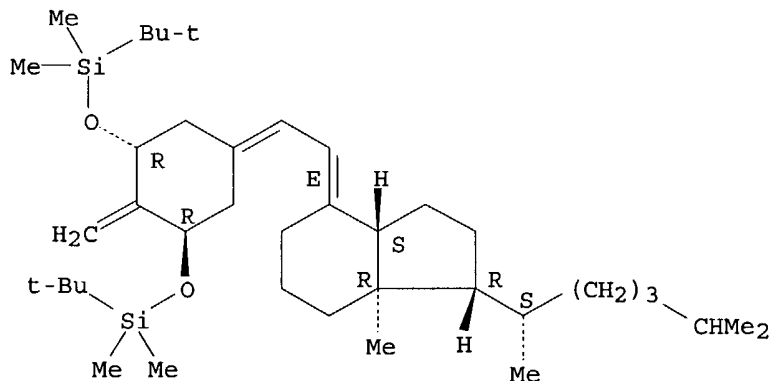
(nor-vitamin D3 derivs. and pharmaceutical uses)

RN 618104-22-6 USPATFULL

CN Silane, [[(1 α ,3 β ,7E,20S)-2-methylene-19-nor-9,10-secocholesta-5,7,10(19)-triene-1,3-diyl]bis(oxy)]bis(1,1-dimethylethyl)dimethyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



L10 ANSWER 5 OF 18 USPATFULL on STN

AN 2004:197370 USPATFULL

TI (20S)-1 α -hydroxy-2 α -methyl and 2 β -methyl-19-nor-vitamin D3 and their uses

IN DeLuca, Hector F., Deerfield, WI, UNITED STATES

Sicinski, Rafal R., Warsaw, POLAND

Grzywacz, Pawel K., Madison, WI, UNITED STATES

PA Wisconsin Alumni Research Foundation, Madison, WI (U.S. corporation)

PI US 2004152676 A1 20040805

AI US 2004-762710 A1 20040122 (10)

RLI Division of Ser. No. US 2002-127180, filed on 22 Apr 2002, PENDING

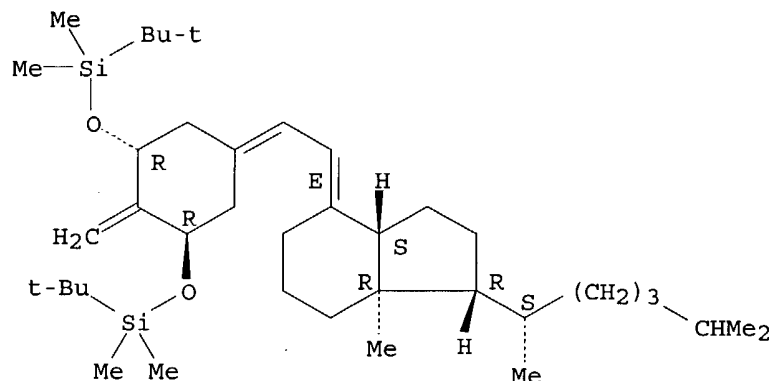
DT Utility

FS APPLICATION

AB This invention discloses (20S)-1 α -hydroxy-2 α -methyl-19-nor-vitamin D.sub.3 and (20S)-1 α -hydroxy-2 β -methyl-19-nor-vitamin D.sub.3 and pharmaceutical uses therefor. These compounds exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as an anti-cancer agent and for the treatment of skin diseases such as psoriasis as well as skin conditions such as wrinkles, slack skin, dry skin and insufficient sebum secretion. These compounds also have very significant calcemic activity and therefore may be used to treat immune disorders in humans as well as metabolic bone diseases such as osteoporosis.

CN Silane, [(1 α ,3 β ,7E,20S)-2-methylene-19-nor-9,10-secocholesta-5,7,10(19)-triene-1,3-diyl]bis(oxy)]bis(1,1-dimethylethyl)dimethyl-
(9CI) (CA INDEX NAME)

Double bond geometry as shown.



LREP ANDRUS, SCEALES, STARKE & SAWALL, LLP, 100 EAST WISCONSIN AVENUE, SUITE
1100, MILWAUKEE, WI, 53202

CLMN Number of Claims: 77
 ECL Exemplary Claim: 1
 DRWN 1 Drawing Page(s)
 LN.CNT 977

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention discloses (20S)-1 α -hydroxy-2 α -methyl-19-nor-vitamin D.sub.3 and (20S)-1 α -hydroxy-2 β -methyl-19-nor-vitamin D.sub.3 and pharmaceutical uses therefor. These compounds exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as an anti-cancer agent and for the treatment of skin diseases such as psoriasis as well as skin conditions such as wrinkles, slack skin, dry skin and insufficient sebum secretion. These compounds also have very significant calcemic activity and therefore may be used to treat immune disorders in humans as well as metabolic bone diseases such as osteoporosis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

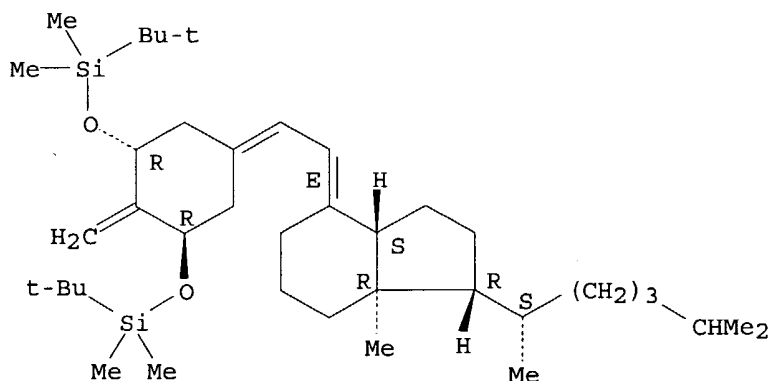
IT 618104-22-6P

(nor-vitamin D3 derivs. and pharmaceutical uses)

RN 618104-22-6 USPATFULL

CN Silane, [[(1 α ,3 β ,7E,20S)-2-methylene-19-nor-9,10-secocholesta-5,7,10(19)-triene-1,3-diyl]bis(oxy)]bis(1,1-dimethylethyl)dimethyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.



L10 ANSWER 7 OF 18 USPATFULL on STN

AN 2004:45005 USPATFULL

TI (20S)-1 α -hydroxy-2-methylene-19-nor-bishomopregnacalciferol and its uses

IN DeLuca, Hector F., Deerfield, WI, UNITED STATES

Plum, Lori A., Madison, WI, UNITED STATES

Clagett-Dame, Margaret, Madison, WI, UNITED STATES

PA Wisconsin Alumni Research Foundation, Madison, WI, UNITED STATES (U.S. corporation)

PI US 2004033998 A1 20040219

AI US 2003-462272 A1 20030616 (10)

RLI Division of Ser. No. US 2002-78204, filed on 18 Feb 2002, GRANTED, Pat. No. US 6627622

DT Utility

FS APPLICATION

LREP ANDRUS, SCEALES, STARKE & SAWALL, LLP, 100 EAST WISCONSIN AVENUE, SUITE 1100, MILWAUKEE, WI, 53202

CLMN Number of Claims: 33

LN.CNT 500

AB This invention discloses (20S)-1 α -hydroxy-2-methylene-19-nor-bishomopregnacalciferol and pharmaceutical uses therefor. This compound exhibits pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as an anti-cancer agent and for the treatment of skin diseases such as psoriasis as well as skin conditions such as wrinkles, slack skin, dry skin and insufficient sebum secretion. This compound also has little, if any, calcemic activity and therefore may be used to treat immune disorders in humans as well as renal osteodystrophy.

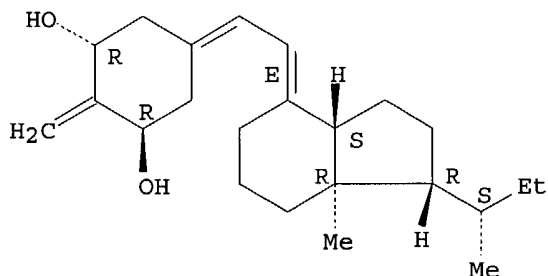
IT 524067-21-8, (20S)-1 α -Hydroxy-2-methylene-19-norbishomopregnacalciferol

((20S)-1 α -hydroxy-2-methylene-19-nor-bishomopregnacalciferol and its therapeutic applications in the treatment of cancer, skin diseases and immune disorders)

RN 524067-21-8 USPATFULL

CN 1,3-Cyclohexanediol, 2-methylene-5-[(2E)-[(1R,3aS,7aR)-octahydro-7a-methyl-1-[(1S)-1-methylpropyl]-4H-inden-4-ylidene]ethylidene]-, (1R,3R)- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



AN 2003:289341 USPATFULL

TI 2-Methylene-19-nor-20(S)-1 α -hydroxy-bis-homo-pregnacalciferol in crystalline form

IN DeLuca, Hector F., Deerfield, WI, UNITED STATES
Thoden, James B., Madison, WI, UNITED STATES
Holden, Hazel M., Fitchburg, WI, UNITED STATES
Clagett-Dame, Margaret, Deerfield, WI, UNITED STATES
Gowlugari, Sumithra, Madison, WI, UNITED STATES
Grzywacz, Pawel, Madison, WI, UNITED STATES

PI	US	2003204103	A1	20031030
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AI US 2002-317467 A1 20021212 (10)

PRAI US 2001-341138P 20011213 (60)

DT Utility

FS	APPLICATION
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LREP ANDRUS, SCEALES, STARKE & SAWALL, LLP, 100 EAST WISCONSIN AVENUE, SUITE
1100, MILWAUKEE, WI, 53202

CLMN Number of Claims: 9

ECL Exemplary Claim: 1

DRWN 1 Drawing Page(s)

LN.CNT 2169

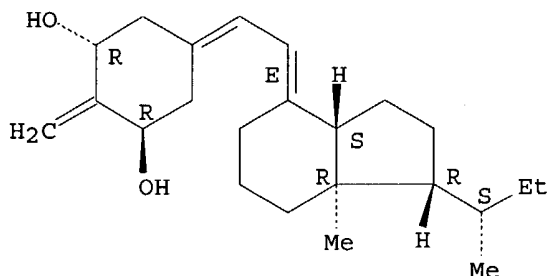
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A method of purifying 2-methylene-19-nor-20(S)-1 α -hydroxy-bis-homo-pregnacalCIFerol to obtain 2-methylene-19-nor-20(S)-1 α -hydroxy-bis-homo-pregnacalCIFerol in crystalline form. The method includes the steps of boiling a solvent such as acetone under inert atmosphere, dissolving a product containing 2-methylene-19-nor-20(S)-1 α -hydroxy-bis-homo-pregnacalCIFerol to be purified in the solvent, cooling the solvent and dissolved product below ambient temperature for a sufficient amount of time to form a precipitate of 2-methylene-19-nor-20(S)-1 α -hydroxy-bis-homo-pregnacalCIFerol crystals, and recovering the 2-methylene-19-nor-20(S)-1 α -hydroxy-bis-homo-pregnacalCIFerol crystals.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT **524067-21-8**, (20S)-1 α -Hydroxy-2-methylene-19-norbishomopregnacalCIFerol
 ((20S)-1 α -hydroxy-2-methylene-19-nor-bishomopregnacalCIFerol and its therapeutic applications in the treatment of cancer, skin diseases and immune disorders)
 RN 524067-21-8 USPATFULL
 CN 1,3-Cyclohexanediol, 2-methylene-5-[(2E)-[(1R,3aS,7aR)-octahydro-7a-methyl-1-[(1S)-1-methylpropyl]-4H-inden-4-ylidene]ethylidene]-, (1R,3R)- (9CI)
 (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.



L10 ANSWER 9 OF 18 USPATFULL on STN

AN 2003:289123 USPATFULL

TI (20S) 1 α -hydroxy-2 α -methyl and 2 β -methyl-19-nor-vitamin D₃ and their uses

IN DeLuca, Hector F., Deerfield, WI, UNITED STATES

Sicinski, Rafal R., Warsaw, POLAND

Grzywacz, Pawel K., Madison, WI, UNITED STATES

PI US 2003203882 A1 20031030

AI US 2002-127180 A1 20020422 (10)

DT Utility

FS APPLICATION

LREP KINNEY & LANGE, P.A., THE KINNEY & LANGE BUILDING, 312 SOUTH THIRD STREET, MINNEAPOLIS, MN, 55415-1002

CLMN Number of Claims: 77

ECL Exemplary Claim: 1

DRWN 1 Drawing Page(s)

LN.CNT 979

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention discloses (20S)-1 α -hydroxy-2 α -methyl-19-nor-vitamin D₃ and (20S)-1 α -hydroxy-2 β -methyl-19-nor-vitamin D₃ and pharmaceutical uses therefor. These compounds exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing

use as an anti-cancer agent and for the treatment of skin diseases such as psoriasis as well as skin conditions such as wrinkles, slack skin, dry skin and insufficient sebum secretion. These compounds also have very significant calcemic activity and therefore may be used to treat immune disorders in humans as well as metabolic bone diseases such as osteoporosis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 618104-22-6P

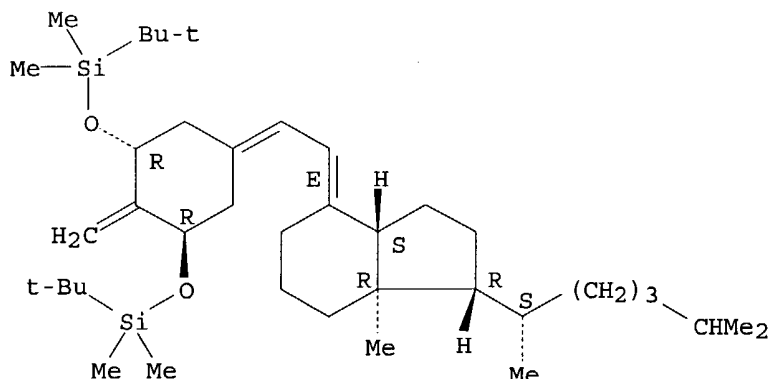
(nor-vitamin D3 derivs. and pharmaceutical uses)

RN 618104-22-6 USPATFULL

CN Silane, [[(1 α ,3 β ,7E,20S)-2-methylene-19-nor-9,10-secocholesta-5,7,10(19)-triene-1,3-diyl]bis(oxy)]bis(1,1-dimethylethyl)dimethyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



L10 ANSWER 10 OF 18 USPATFULL on STN

AN 2003:271487 USPATFULL

TI Method of synthesizing 1 α -hydroxy-2-methylene-19-nor-homopregnacalciferol

IN DeLuca, Hector F., Deerfield, WI, UNITED STATES

Gowlugari, Sumithra, Fremont, CA, UNITED STATES

Sicinski, Rafal R., Warsaw, POLAND

PI US 2003191095 A1 20031009

US 6774251 B2 20040810

AI US 2003-397135 A1 20030326 (10)

PRAI US 2002-369159P 20020329 (60)

DT Utility

FS APPLICATION

LREP ANDRUS, SCEALES, STARKE & SAWALL, LLP, 100 EAST WISCONSIN AVENUE, SUITE 1100, MILWAUKEE, WI, 53202

CLMN Number of Claims: 15

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 423

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A method of making 1 α -hydroxy-2-methylene-19-nor-homopregnacalciferol. The method includes the steps of condensing a bicyclic ketone with an allylic phosphine oxide to produce a protected 19-nor-pregnacalciferol analog, thereafter cleaving the protecting group to form 22-alcohol, converting the alcohol to an ester, reducing the ester to 17 β -isopropyl-19-nor-vitamin D analog, and finally deprotecting the 17 β -isopropyl derivative to form the desired compound.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

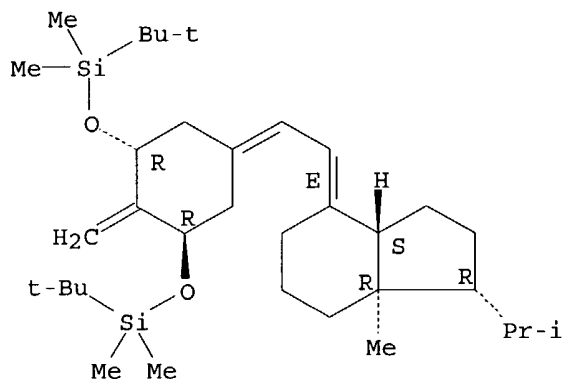
IT 610304-71-7P

(preparation of 1 α -hydroxy-2-methylene-19-nor-homopregnacalciferol
from vitamin D2)

RN 610304-71-7 USPTFULL

CN Silane, [[(1R,3R)-2-methylene-5-[(2E)-[(1R,3aS,7aR)-octahydro-7a-methyl-1-(1-methylethyl)-4H-inden-4-ylidene]ethylidene]-1,3-cyclohexanediyl]bis(oxy)]bis[(1,1-dimethylethyl)dimethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



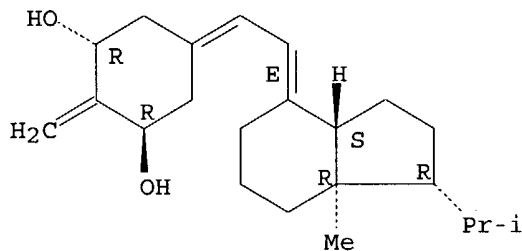
IT 524067-22-9P

(preparation of 1 α -hydroxy-2-methylene-19-nor-homopregnacalciferol
from vitamin D2)

RN 524067-22-9 USPTFULL

CN 1,3-Cyclohexanediol, 2-methylene-5-[(2E)-[(1R,3aS,7aR)-octahydro-7a-methyl-1-(1-methylethyl)-4H-inden-4-ylidene]ethylidene]-, (1R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L10 ANSWER 11 OF 18 USPTFULL on STN

AN 2003:226344 USPTFULL

TI (20S)-1ALPHA-HYDROXY-2-METHYLENE-19-NOR-BISHOMOPREGNACALCIFEROL AND ITS
USES

IN DeLuca, Hector F., Deerfield, WI, UNITED STATES

Plum, Lori A., Madison, WI, UNITED STATES

Clagett-Dame, Margaret, Madison, WI, UNITED STATES

PI US 2003158157 A1 20030821

US 6627622 B2 20030930

AI US 2002-78204 A1 20020218 (10)

DT Utility
 FS APPLICATION
 LREP ANDRUS, SCEALES, STARKE & SAWALL, LLP, 100 EAST WISCONSIN AVENUE, SUITE
 1100, MILWAUKEE, WI, 53202
 CLMN Number of Claims: 33
 ECL Exemplary Claim: 1
 DRWN 6 Drawing Page(s)
 LN.CNT 500

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

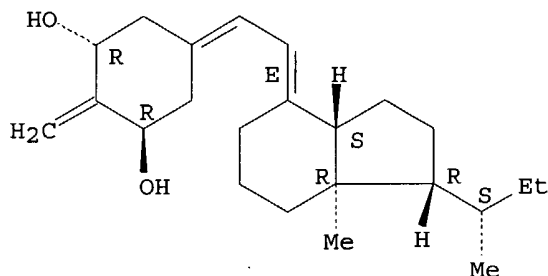
AB This invention discloses (20S)-1 α -hydroxy-2-methylene-19-nor-bishomopregnacalciferol and pharmaceutical uses therefor. This compound exhibits pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as an anti-cancer agent and for the treatment of skin diseases such as psoriasis as well as skin conditions such as wrinkles, slack skin, dry skin and insufficient sebum secretion. This compound also has little, if any, calcemic activity and therefore may be used to treat immune disorders in humans as well as renal osteodystrophy.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 524067-21-8, (20S)-1 α -Hydroxy-2-methylene-19-norbishomopregnacalciferol
 ((20S)-1 α -hydroxy-2-methylene-19-nor-bishomopregnacalciferol and its therapeutic applications in the treatment of cancer, skin diseases and immune disorders)
 RN 524067-21-8 USPTAFULL
 CN 1,3-Cyclohexanediol, 2-methylene-5-[(2E)-[(1R,3aS,7aR)-octahydro-7a-methyl-1-[(1S)-1-methylpropyl]-4H-inden-4-ylidene]ethylidene]-, (1R,3R)- (9CI)
 (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



L10 ANSWER 12 OF 18 USPTAFULL on STN
 AN 2003:137075 USPTAFULL
 TI 1 α -hydroxy-2-methylene-19-nor-pregnacalciferol and its uses
 IN DeLuca, Hector F., Deerfield, WI, United States
 Plum, Lori A., Madison, WI, United States
 Clagett-Dame, Margaret, Madison, WI, United States
 PA Wisconsin Alumni Research Foundation, Madison, WI, United States (U.S. corporation)
 PI US 6566352 B1 20030520
 AI US 2002-77916 20020218 (10)
 DT Utility
 FS GRANTED
 EXNAM Primary Examiner: Qazi, Sabiha
 LREP Andrus, Sceales, Starke & Sawall, LLP
 CLMN Number of Claims: 33
 ECL Exemplary Claim: 1

DRWN 14 Drawing Figure(s); 6 Drawing Page(s)

LN.CNT 494

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention discloses 1α -hydroxy-2-methylene-19-nor-pregnacalciferol and pharmaceutical uses therefor. This compound exhibits pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as an anti-cancer agent and for the treatment of skin diseases such as psoriasis as well as skin conditions such as wrinkles, slack skin, dry skin and insufficient sebum secretion. This compound also has little, if any, calcemic activity and therefore may be used to treat immune disorders in humans as well as renal osteodystrophy.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 524067-21-8 524067-22-9

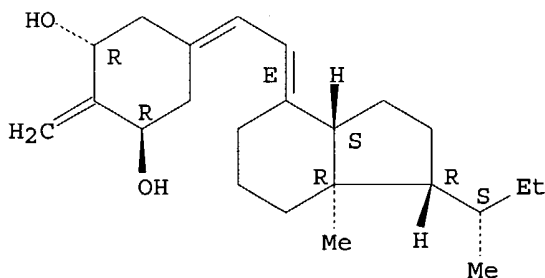
(effects of vitamin D compds. on cell differentiation and calcium levels in relation to their potential pharmaceutical uses)

RN 524067-21-8 USPATFULL

CN 1,3-Cyclohexanediol, 2-methylene-5-[(2E)-[(1R,3aS,7aR)-octahydro-7a-methyl-1-[(1S)-1-methylpropyl]-4H-inden-4-ylidene]ethylidene]-, (1R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

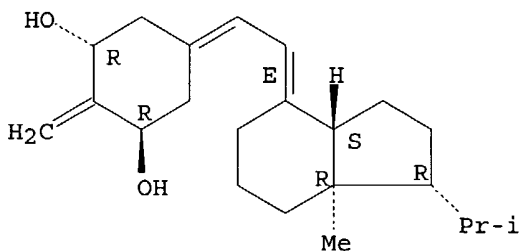


RN 524067-22-9 USPATFULL

CN 1,3-Cyclohexanediol, 2-methylene-5-[(2E)-[(1R,3aS,7aR)-octahydro-7a-methyl-1-(1-methylethyl)-4H-inden-4-ylidene]ethylidene]-, (1R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



IT 524067-20-7

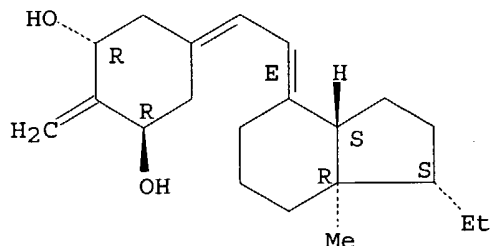
(methods for using 1α -Hydroxy-2-methylene-19-nor-pregnacalciferol in treatment of cancer, skin diseases and immune disorders)

RN 524067-20-7 USPATFULL

CN 1,3-Cyclohexanediol, 5-[(2E)-[(1S,3aS,7aR)-1-ethyloctahydro-7a-methyl-4H-inden-4-ylidene]ethylidene]-2-methylene-, (1R,3R)- (9CI) (CA INDEX NAME)

NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L10 ANSWER 13 OF 18 USPATFULL on STN
 AN 2002:323123 USPATFULL
 TI 1α-hydroxy-2-methylene-19-nor-homopregnacalciferol and its uses
 IN DeLuca, Hector F., Deerfield, WI, UNITED STATES
 Sicinski, Rafal R., Warsaw, POLAND
 Gowlugari, Sumithra, Madison, WI, UNITED STATES
 Plum, Lori A., Madison, WI, UNITED STATES
 Clagett-Dame, Margaret, Deerfield, WI, UNITED STATES
 PA Wisconsin Alumni Research Foundation of Madison (U.S. corporation)
 PI US 2002183289 A1 20021205
 US 6579861 B2 20030617
 AI US 2002-165123 A1 20020607 (10)
 RLI Division of Ser. No. US 2001-878438, filed on 11 Jun 2001, GRANTED, Pat.
 No. US 6440953 Continuation-in-part of Ser. No. US 2000-657828, filed on
 8 Sep 2000, ABANDONED
 DT Utility
 FS APPLICATION
 LREP ANDRUS, SCEALES, STARKE & SAWALL, LLP, 100 EAST WISCONSIN AVENUE, SUITE
 1100, MILWAUKEE, WI, 53202
 CLMN Number of Claims: 33
 ECL Exemplary Claim: 1
 DRWN 7 Drawing Page(s)
 LN.CNT 503

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention discloses 1α-hydroxy-2-methylene-19-nor-homopregnacalciferol and pharmaceutical uses therefor. This compound exhibits pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as an anti-cancer agent and for the treatment of skin diseases such as psoriasis as well as skin conditions such as wrinkles, slack skin, dry skin and insufficient sebum secretion. This compound also has little, if any, calcemic activity and therefore may be used to treat immune disorders in humans as well as renal osteodystrophy.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

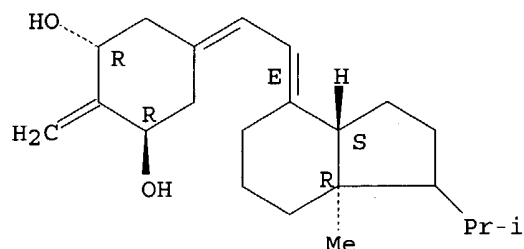
IT 403647-27-8

(1α-hydroxy-2-methylene-19-nor-homopregnacalciferol and
therapeutic applications)

RN 403647-27-8 USPATFULL

CN 1,3-Cyclohexanediol, 2-methylene-5-[(2E)-[(3aS,7aR)-octahydro-7a-methyl-1-(1-methylethyl)-4H-inden-4-ylidene]ethylidene]-, (1R,3R)- (9CI) (CA
INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L10 ANSWER 14 OF 18 USPATFULL on STN

AN 2002:99449 USPATFULL

TI 1alpha-hydroxy-2-methylene-19-nor-homopregnacalciferol and its uses

IN DeLuca, Hector F., Deerfield, WI, UNITED STATES

Sicinski, Rafal R., Warsaw, POLAND

Gowlugari, Sumithra, Madison, WI, UNITED STATES

Plum, Lori A., Madison, WI, UNITED STATES

Clagett-Dame, Margaret, Deerfield, WI, UNITED STATES

PI US 2002052350 A1 20020502

US 6440953 B2 20020827

AI US 2001-878438 A1 20010611 (9)

RLI Continuation-in-part of Ser. No. US 2000-657828, filed on 8 Sep 2000,
PENDING

DT Utility

FS APPLICATION

LREP Thomas M. Wozny, ANDRUS, SCEALES, STARKE & SAWALL, LLP, 100 East
Wisconsin Avenue, Suite 1100, Milwaukee, WI, 53202-4178

CLMN Number of Claims: 33

ECL Exemplary Claim: 1

DRWN 7 Drawing Page(s)

LN.CNT 502

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention discloses 1 α -hydroxy-2-methylene-19-nor-homopregnacalciferol and pharmaceutical uses therefor. This compound exhibits pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as an anti-cancer agent and for the treatment of skin diseases such as psoriasis as well as skin conditions such as wrinkles, slack skin, dry skin and insufficient sebum secretion. This compound also has little, if any, calcemic activity and therefore may be used to treat immune disorders in humans as well as renal osteodystrophy.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 403647-27-8

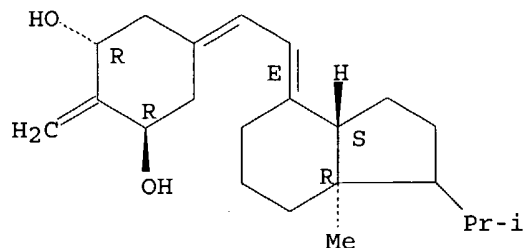
(hydroxymethylenenorhomopregnacalciferol and therapeutic use)

RN 403647-27-8 USPATFULL

CN 1,3-Cyclohexanediol, 2-methylene-5-[(2E)-[(3aS,7aR)-octahydro-7a-methyl-1-(1-methylethyl)-4H-inden-4-ylidene]ethylidene]-, (1R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



L10 ANSWER 15 OF 18 USPAT2 on STN

AN 2003:271487 USPAT2

TI Method of synthesizing 1 α -hydroxy-2-methylene-19-nor-homopregnacalciferol

IN DeLuca, Hector F., Deerfield, WI, United States

Gowlugari, Sumithra, Fremont, WI, United States

Sicinski, Rafal R., Warsaw, POLAND

PA Wisconsin Alumni Research Foundation, Madison, WI, United States (U.S. corporation)

PI US 6774251 B2 20040810

AI US 2003-397135 20030326 (10)

PRAI US 2002-369159P 20020329 (60)

DT Utility

FS GRANTED

EXNAM Primary Examiner: Qazi, Sabiha

LREP Andrus, Sceales, Starke & Sawall, LLP

CLMN Number of Claims: 15

ECL Exemplary Claim: 1

DRWN 0 Drawing Figure(s); 0 Drawing Page(s)

LN.CNT 433

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A method of making 1 α -hydroxy-2-methylene-19-nor-homopregnacalciferol. The method includes the steps of condensing a bicyclic ketone with an allylic phosphine oxide to produce a protected 19-nor-pregnacalciferol analog, thereafter cleaving the protecting group to form 22-alcohol, converting the alcohol to an ester, reducing the ester to 17 β -isopropyl-19-nor-vitamin D analog, and finally deprotecting the 17 β -isopropyl derivative to form the desired compound.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 610304-71-7P

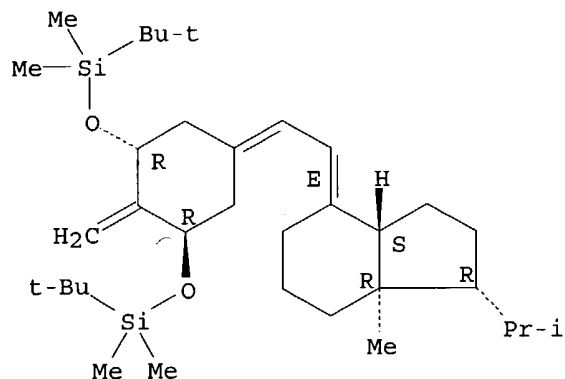
(preparation of 1 α -hydroxy-2-methylene-19-nor-homopregnacalciferol from vitamin D2)

RN 610304-71-7 USPAT2

CN Silane, [[(1R,3R)-2-methylene-5-[(2E)-[(1R,3aS,7aR)-octahydro-7a-methyl-1-(1-methylethyl)-4H-inden-4-ylidene]ethylidene]-1,3-cyclohexanediyl]bis(oxy)]bis[(1,1-dimethylethyl)dimethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



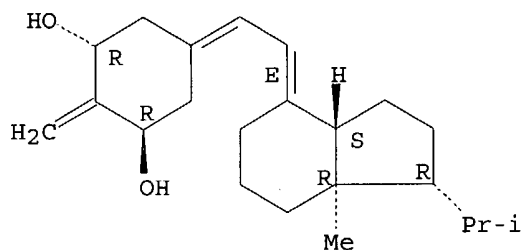
IT 524067-22-9P

(preparation of 1 α -hydroxy-2-methylene-19-nor-homopregnacalciferol
from vitamin D2)

RN 524067-22-9 USPAT2

CN 1,3-Cyclohexanediol, 2-methylene-5-[(2E)-[(1R,3aS,7aR)-octahydro-7a-methyl-
1-(1-methylethyl)-4H-inden-4-ylidene]ethylidene]-, (1R,3R)- (9CI) (CA
INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L10 ANSWER 16 OF 18 USPAT2 on STN

AN 2003:226344 USPAT2

TI (20S)-1 α -hydroxy-2-methylene-19-nor-bishomopregnacalciferol and
its uses

IN DeLuca, Hector F., Deerfield, WI, United States

Plum, Lori A., Madison, WI, United States

Clagett-Dame, Margaret, Madison, WI, United States

PA Wisconsin Alumni Research Foundation, Madison, WI, United States (U.S.
corporation)

PI US 6627622 B2 20030930

AI US 2002-78204 20020218 (10)

DT Utility

FS GRANTED

EXNAM Primary Examiner: Padmanabhan, Sreeni; Assistant Examiner: Hui, San-ming

LREP Andrus, Sceales, Starke & Sawall, LLP

CLMN Number of Claims: 1

ECL Exemplary Claim: 1

DRWN 14 Drawing Figure(s); 6 Drawing Page(s)

LN.CNT 419

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention discloses (20S)-1 α -hydroxy-2-methylene-19-nor-
bishomopregnacalciferol and pharmaceutical uses therefor. This compound
exhibits pronounced activity in arresting the proliferation of

undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as an anti-cancer agent and for the treatment of skin diseases such as psoriasis as well as skin conditions such as wrinkles, slack skin, dry skin and insufficient sebum secretion. This compound also has little, if any, calcemic activity and therefore may be used to treat immune disorders in humans as well as renal osteodystrophy.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

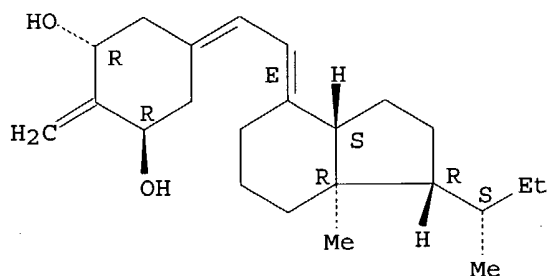
IT 524067-21-8, (20S)-1 α -Hydroxy-2-methylene-19-norbishomopregnacalciferol

((20S)-1 α -hydroxy-2-methylene-19-nor-bishomopregnacalciferol and its therapeutic applications in the treatment of cancer, skin diseases and immune disorders)

RN 524067-21-8 USPAT2

CN 1,3-Cyclohexanediol, 2-methylene-5-[(2E)-[(1R,3aS,7aR)-octahydro-7a-methyl-1-[(1S)-1-methylpropyl]-4H-inden-4-ylidene]ethylidene]-, (1R,3R)- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L10 ANSWER 17 OF 18 USPAT2 on STN

AN 2002:323123 USPAT2

TI 1 α -hydroxy-2-methylene-19-nor-homopregnacalciferol and its uses

IN DeLuca, Hector F., Deerfield, WI, United States

Sicinski, Rafal R., Warsaw, POLAND

Gowlugari, Sumithra, Madison, WI, United States

Plum, Lori A., Madison, WI, United States

Clagett-Dame, Margaret, Deerfield, WI, United States

PA Wisconsin Alumni Research Foundation, Madison, WI, United States (U.S. corporation)

PI US 6579861 B2 20030617

AI US 2002-165123 20020607 (10)

RLI Division of Ser. No. US 2001-878438, filed on 11 Jun 2001, now patented, Pat. No. US 6440953 Continuation-in-part of Ser. No. US 2000-657828, filed on 8 Sep 2000, now abandoned

DT Utility

FS GRANTED

EXNAM Primary Examiner: Qazi, Sabiha

LREP Andrus, Sceales, Starke & Sawall, LLP

CLMN Number of Claims: 7

ECL Exemplary Claim: 1

DRWN 7 Drawing Figure(s); 7 Drawing Page(s)

LN.CNT 432

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention discloses 1 α -hydroxy-2-methylene-19-nor-homopregnacalciferol and pharmaceutical uses therefor. This compound exhibits pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the

monocyte thus evidencing use as an anti-cancer agent and for the treatment of skin diseases such as psoriasis as well as skin conditions such as wrinkles, slack skin, dry skin and insufficient sebum secretion. This compound also has little, if any, calcemic activity and therefore may be used to treat immune disorders in humans as well as renal osteodystrophy.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

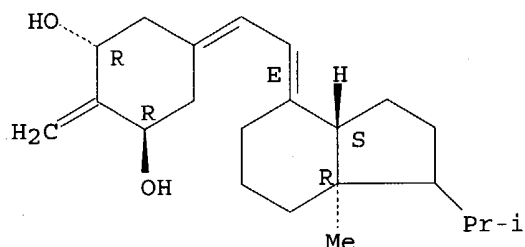
IT 403647-27-8

(1 α -hydroxy-2-methylene-19-nor-homopregnacalciferol and therapeutic applications)

RN 403647-27-8 USPAT2

CN 1,3-Cyclohexanediol, 2-methylene-5-[(2E)-[(3aS,7aR)-octahydro-7a-methyl-1-(1-methylethyl)-4H-inden-4-ylidene]ethylidene]-, (1R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L10 ANSWER 18 OF 18 USPAT2 on STN

AN 2002:99449 USPAT2

TI 1 α -hydroxy-2-methylene-19-nor-homopregnacalciferol and its uses

IN DeLuca, Hector F., Deerfield, WI, United States

Sicinski, Rafal R., Warsaw, POLAND

Gowlugari, Sumithra, Madison, WI, United States

Plum, Lori A., Madison, WI, United States

Clagett-Dame, Margaret, Deerfield, WI, United States

PA Wisconsin Alumni Research Foundation, Madison, WI, United States (U.S. corporation)

PI US 6440953 B2 20020827

AI US 2001-878438 20010611 (9)

RLI Continuation-in-part of Ser. No. US 2000-657828, filed on 8 Sep 2000

DT Utility

FS GRANTED

EXNAM Primary Examiner: Qazi, Sabiha

LREP Andrus, Sceales, Starke & Sawall, LLP

CLMN Number of Claims: 26

ECL Exemplary Claim: 1

DRWN 7 Drawing Figure(s); 7 Drawing Page(s)

LN.CNT 485

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention discloses 1 α -hydroxy-2-methylene-19-nor-homopregnacalciferol and pharmaceutical uses therefor. This compound exhibits pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as an anticancer agent and for the treatment of skin diseases such as psoriasis as well as skin conditions such as wrinkles, slack skin, dry skin and insufficient sebum secretion. This compound also has little, if any, calcemic activity and therefore may be used to treat immune disorders in humans as well as renal osteodystrophy.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 403647-27-8

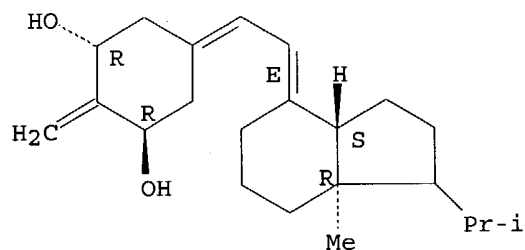
(hydroxymethylenenorhomopregnacalciferol and therapeutic use)

RN 403647-27-8 USPAT2

CN 1,3-Cyclohexanediol, 2-methylene-5-[(2E)-[(3aS,7aR)-octahydro-7a-methyl-1-(1-methylethyl)-4H-inden-4-ylidene]ethylidene]-, (1R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



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FILE 'REGISTRY' ENTERED AT 13:53:01 ON 25 AUG 2004

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STRUCTURE FILE UPDATES: 24 AUG 2004 HIGHEST RN 732209-96-0

DICTIONARY FILE UPDATES: 24 AUG 2004 HIGHEST RN 732209-96-0

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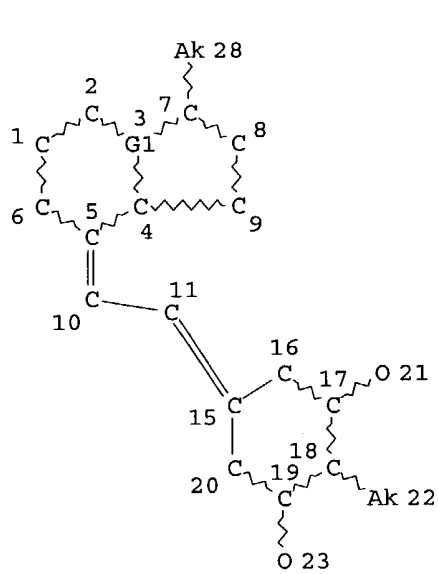
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Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
<http://www.cas.org/ONLINE/DBSS/registryss.html>

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L1 STR



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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

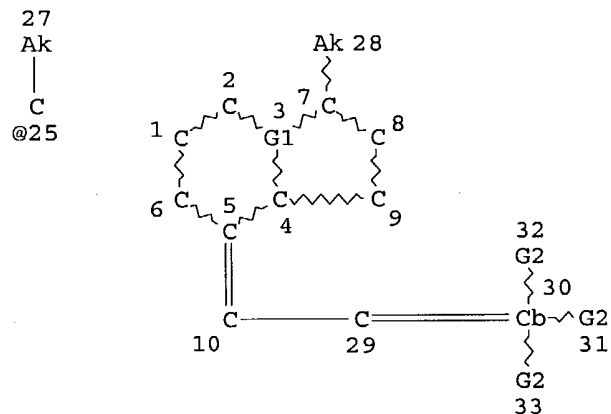
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NUMBER OF NODES IS 23

STEREO ATTRIBUTES: NONE

L2 8 SEA FILE=REGISTRY CSS FUL L1

L3 STR



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VAR G2=OH/AK

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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RSPEC 5

NUMBER OF NODES IS 18

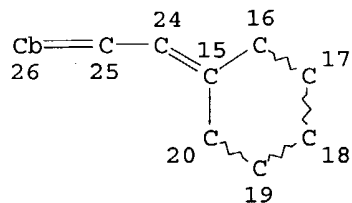
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NOT 46.150.18/RID

L7 136 SEA FILE=REGISTRY SUB=L5 CSS FUL L3

L8 130 SEA FILE=REGISTRY ABB=ON PLU=ON L7 NOT L2

L9 STR



NODE ATTRIBUTES:

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CONNECT IS M1 RC AT 18

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CONNECT IS M1 RC AT 26

DEFAULT MLEVEL IS ATOM

GGCAT IS PCY AT 26

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RSPEC 19

NUMBER OF NODES IS 9

STEREO ATTRIBUTES: NONE

L11 0 SEA FILE=REGISTRY SUB=L8 CSS FUL L9

100.0% PROCESSED 130 ITERATIONS

0 ANSWERS

SEARCH TIME: 00.00.01

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